2D01

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: P Spivack Examiner # : 70406 Date: 12/4/02
Art Unit: 1614 Phone Number 30 84703 Serial Number: 10/074595
Mail Box and Bldg/Room Location: 2D05 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: α-Aryl-N-Alkylnitrones

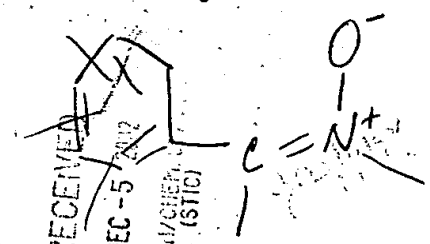
Inventors (please provide full names): Judith A. Kelleher
Kirk R. Maples

Earliest Priority Filing Date: 10/15/98

Mary Hale – Supervisor, Info. Branch
STIC – Biotech/Chem. Library
CM-1 Room E01
703-308-4258

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search:
methods for ameliorating a neurodegenerative disease and
an autoimmune disease (as lupus or MS)
comprising administering a compound of



C20.111

(Alzheimer's, Parkinson's, HIV dementia
auto antibodies
auto immunity
graves addison
- degenerative neurologic disease
arthritis
Reiter
thyroiditis
proteoglycan
amyloid fibril protein
amyloid beta protein precursor
degenerat? (a) neurol? disease (a) degen?
appican
APP-proteolysis
paralysis agit
Lewy bodies
MS
AIDS encephalopath?
dementia complex (a) AIDS

alkylenedioxy
may form a ring
RECEIVED DEC -5
TECHNOLOGY CENTER (STIC)

No other heterocycles.

Thanks

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Mary	NA Sequence (#)	STN 5.29 1.89
Searcher Phone #:	AA Sequence (#)	Dialog 8.28
Searcher Location:	Structure (#) 1	Questel/Orbit 7.25
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed: 12/10	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems 14T.60
Clerical Prep Time:	Patent Family	WWW/Internet 5 146.27
Online Time: 67	Other	Other (specify) 5291.89

PTO-1590 (8-01)

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L3 63 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 71420 ITERATIONS 63 ANSWERS
SEARCH TIME: 00.00.01

=> fil medl,hcap,biosis,embase,jicst;s l3 and (neurodegenerat? or degenerat?(a)neurolog? or neurolog? disease(a)degenerat? or degenerat?(a)(nervous system or cns or central nervous system))

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	145.60	350.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.29

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L4 0 FILE MEDLINE
L5 0 FILE HCAPLUS
L6 0 FILE BIOSIS
L7 0 FILE EMBASE
L8 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L9 0 L3 AND (NEURODEGENERAT? OR DEGENERAT?(A) NEUROLOG? OR NEUROLOG? DISEASE(A) DEGENERAT? OR DEGENERAT?(A)(NERVOUS SYSTEM OR CNS OR CENTRAL NERVOUS SYSTEM))

=> s l3 and (alzheimer? pr parkinson? or hiv dementia or human immunodeficiency virus dementia)
L10 0 FILE MEDLINE
L11 0 FILE HCAPLUS
<------User Break------>

SEARCH ENDED BY USER

=> s l3 and (alzheimer? or parkinson? or hiv dementia or human immunodeficiency virus dementia)

Searched by: Mary Hale 308-4258 CM-1 1E01

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L15             0 FILE BIOSIS
L16             0 FILE EMBASE
L17             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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                  DEFICIENCY VIRUS DEMENTIA)

=> s l3 and (proteoglycan? or amyloid fibril protein or amyloid beta protein
precursor or appican or app-proteoglycan or paralysis agitans or lewy odies or
(aids or hiv)(a)encephalopath? or dementia complex(a)(aids or hiv))
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L23             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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                  AGITANS OR LEWY ODIES OR (AIDS OR HIV)(A) ENCEPHALOPATH? OR
                  DEMENTIA COMPLEX(A)(AIDS OR HIV))

=> s l3 and (automimmun?(a)(disease or disorder) or autoimmunity or autoantibod? or
lupus or ms or multiple sclerosis or arthritis or purpura or reiter or thyroiditis
or grave? or addison?)
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L28             0 FILE EMBASE
L29             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L30             0 L3 AND (AUTOMIMMUN?(A)(DISEASE OR DISORDER) OR AUTOIMMUNITY OR
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                  OR PURPURA OR REITER OR THYROIDITIS OR GRAVE? OR ADDISON?)

=> s kelleher, j?/au;s maple, k?/au
L31           306 FILE MEDLINE
L32           173 FILE HCAPLUS
L33           387 FILE BIOSIS
L34           245 FILE EMBASE
L35             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L36          1111 KELLEHER, J?/AU


L37             0 FILE MEDLINE
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L39             0 FILE BIOSIS
L40             0 FILE EMBASE
L41             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L42             0 MAPLE, K?/AU

=> s maples, k?/au


Searched by: Mary Hale 308-4258 CM-1 1E01
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L43          21 FILE MEDLINE
L44          42 FILE HCAPLUS
L45          43 FILE BIOSIS
L46          19 FILE EMBASE
L47           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L48         125 MAPLES, K?/AU

=> s l36 and l48
L49           0 FILE MEDLINE
L50           5 FILE HCAPLUS
L51          10 FILE BIOSIS
L52           0 FILE EMBASE
L53           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L54          15 L36 AND L48

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L55           0 FILE MEDLINE
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L57           0 FILE BIOSIS
L58           0 FILE EMBASE
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L60           0 L3 AND L54

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L65           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L66           0 L54 AND ?NITRONES?/CNS
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> s l54 and ?nitrones?


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L68 3 FILE HCAPLUS
L69 2 FILE BIOSIS
L70 0 FILE EMBASE
LEFT TRUNCATION IGNORED FOR '?NITRONES?' FOR FILE 'JICST-EPLUS'
L71 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L72 5 L54 AND ?NITRONES?
Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> dup rem l72
PROCESSING COMPLETED FOR L72
L73 5 DUP REM L72 (0 DUPLICATES REMOVED)

=> d 1-5 cbib abs

L73 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:501988 Document No.: PREV200200501988. alpha-aryl-N-**alkylnitrones** and pharmaceutical compositions containing the same. **Kelleher, Judith A.; Maples, Kirk R.**; Dykman, Alina (1); Zhang, Yong-Kang; Wilcox, Allan L.; Levell, Julian. (1) San Fransisco, CA USA. ASSIGNEE: Centaur Pharmaceuticals, Inc., Sunnyvale, CA, USA. Patent Info.: US 6433008 August 13, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 13, 2002) Vol. 1261, No. 2, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133. Language: English.
AB Disclosed are novel aryl-N-alkylnitrone compounds and pharmaceutical compositions containing such compounds. The disclosed compositions are useful as therapeutics for preventing and/or treating neurodegenerative, autoimmune and inflammatory conditions in mammals and as analytical reagents for detecting free radicals.

L73 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:447082 Document No.: PREV200000447082. alpha-aryl-N-**alkylnitrones** and pharmaceutical compositions containing the same. **Kelleher, Judith A. (1); Maples, Kirk R.**; Dykman, Alina; Zhang, Yong-Kang; Wilcox, Allan L.; Levell, Julian. (1) Fremont, CA USA. ASSIGNEE: Centaur Pharmaceuticals, Inc., Sunnyvale, CA, USA. Patent Info.: US 6046232 April 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 4, 2000) Vol. 1233, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.
AB Disclosed are novel alpha-aryl-N-alkylnitrone compounds and pharmaceutical compositions containing such compounds. The disclosed compositions are useful as therapeutics for preventing and/or treating neurodegenerative, autoimmune and inflammatory conditions in mammals and as analytical reagents for detecting free radicals.

L73 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS
1999:464287 Document No. 131:102186 Preparation of **phenylthiofurylalkylnitrones** for treatment of neurological,

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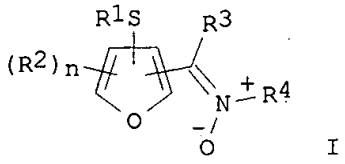
autoimmune, and inflammatory disease and as analytical reagents.. **Kelleher, Judith A.**; **Maples, Kirk R.**; Zhang, Yong-Kang (Centaur Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 9936415 A1 19990722, 59 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US785 19990114. PRIORITY: US 1998-71626 19980116.

GI



I

AB Title compds. [I; R1 = (substituted) alkyl, alkenyl, alkynyl, aralkyl, aryl, cycloalkyl, cycloalkylalkyl, cycloalkenyl; R2 = (substituted) alkyl, alkenyl, alkynyl, aralkyl, aryl, alkoxy, cycloalkyl, halo; R3 = H, (substituted) alkyl, alkenyl, alkynyl, aralkyl, aryl, cycloalkyl, cycloalkylalkyl; R4 = (substituted) alkyl, alkenyl, alkynyl, aralkyl, aryl, cycloalkyl, cycloalkylalkyl, cycloalkenyl; n = 0-2], were prepd. as therapeutics for preventing and/or treating neurodegenerative, autoimmune and inflammatory conditions in mammals and as anal. reagents for detecting free radicals. Thus, 2-(4-methoxyphenylthio)-5-furaldehyde (prepn. given), N-tert-butylhydroxylamine (prepn. given), mol. sieves, and silica gel were refluxed overnight in CHCl3 to give 78.8% .alpha.-[2-(4-methoxyphenylthio)-5-furyl]-N-tert-butylnitrone. I inhibited A.beta.(1-42) .beta.-pleated sheet formation and/or .beta.-amyloid-induced increase of interleukin-1.beta. and/or IL-1.beta.-induced cell toxicity by .gtoreq.30% compared to controls.

L73 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS

1999:282195 Document No. 130:311617 Preparation of .alpha.-aryl-N-**alkylnitrones** for treatment of neurodegenerative, autoimmune, and inflammatory disease and as analytical reagents for detection of free radicals.. **Kelleher, Judith A.**; **Maples, Kirk R.**; Dykman, Alina; Zhang, Yong-Kang; Wilcox, Allan L.; Levell, Julian (Centaur Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 9920601 A1 19990429, 104 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US21624 19981016. PRIORITY: US 1997-62324 19971017; US 1997-63736 19971029; US 1998-90475 19980624.

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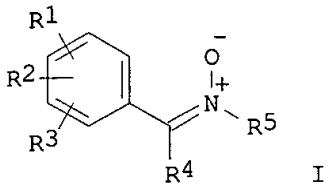

I

AB Title compds. [I; R1 = alkoxy, alkaryloxy, alkcycloalkoxy, aryloxy, cycloalkoxy; R2 = H, alkoxy, alkcycloalkoxy, cycloalkoxy, halo; adjacent R1R2 = alkylenedioxy; R3 = H, alkoxy, alkcycloalkoxy, cycloalkoxy, halo; R4 = H, alkyl; R5 = (substituted) alkyl, cycloalkyl; with provisos], were prepd. Thus, 4-hydroxybenzaldehyde was refluxed 30 min. with NaOH in EtOH; I(CH2)5CH3 was added and the mixt. was refluxed 68 h to give a residue which was kept 18 h with PrNO2, NH4Cl, and Zn in EtOH/H2O to give 12.4% .alpha.-4-hexyloxyphenyl-N-propylnitrone. Several I at 100 mg/kg orally in rats treated with M. tuberculin in incomplete Freunds adjuvant reduced CNS inflammatory deficit.

L73 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
1998:87722 Document No. 128:140602 Furan nitrone compounds. **Kelleher, Judith A.**; **Maples, Kirk R.**; Waterbury, Lowell David; Wilcox, Allan L.; Xu, Hong; Zhang, Yong-kang (Centaur Pharmaceuticals, Inc., USA; Kelleher, Judith A.; Maples, Kirk R.; Waterbury, Lowell David; Wilcox, Allan L.; Xu, Hong; Zhang, Yong-Kang). PCT Int. Appl. WO 9803496 A1 19980129, 99 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US11960 19970714. PRIORITY: US 1996-22169 19960719.

AB Furan **nitrones**, e.g., N-isopropyl-.alpha.-(5-sulfo-2-furanyl)nitrone (I), were prepd. for treatment of neurodegenerative and/or autoimmune disorders. Thus, refluxing N-isopropylhydroxylamine and Na 5-formyl-2-furansulfonate in MeOH gave a 75% yield of I. In rats I reduced the mean infarct vol. of a stroke by 32% when administered 3 h post stroke. Other tests of the **nitrones** included (1) inhibition of A.beta. beta-pleated sheet formation, (2) protection against A.beta.(25-35)-induced neuronal cell loss, (3) inflammation redn., (4) redn. of .beta.-amyloid-induced increased cytokine release, (5) redn. of locomotor impairment due to A.beta.-peptide, (6) redn. of spatial learning deficit, (7) prevention of MBP-induced exptl. allergic encephalomyelitis, (8) prevention of wt. loss, (9) and redn. of learning deficit in autoimmune mice.

=> s l3 and (neurodegener? or autoimmun? or inflamm? or neurolog? or immun?)
L74 0 FILE MEDLINE
L75 0 FILE HCAPLUS
L76 0 FILE BIOSIS
L77 0 FILE EMBASE
L78 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L79 0 L3 AND (NEURODEGENER? OR AUTOIMMUN? OR INFLAMM? OR NEUROLOG? OR

Searched by: Mary Hale 308-4258 CM-1 1E01

IMMUN?)

=> fil reg;d l3 que stat

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	67.22	417.44

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.86	-11.15

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 DEC 2002 HIGHEST RN 475556-62-8
DICTIONARY FILE UPDATES: 9 DEC 2002 HIGHEST RN 475556-62-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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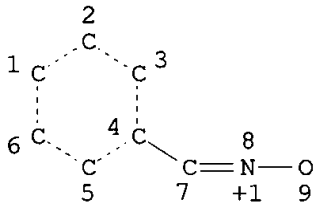

NODE ATTRIBUTES:
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L3 63 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 71420 ITERATIONS 63 ANSWERS
SEARCH TIME: 00.00.01

Searched by: Mary Hale 308-4258 CM-1 1E01

=> d l3 ide can

L3 ANSWER 1 OF 63 REGISTRY COPYRIGHT 2002 ACS
RN 158609-39-3 REGISTRY
CN 5H-Indeno[1,2-b]pyridinium, 5,5-bis[2-(hydroxymethyliminio)-2-phenylethyl]-1-methyl-, triiodide (9CI) (CA INDEX NAME)
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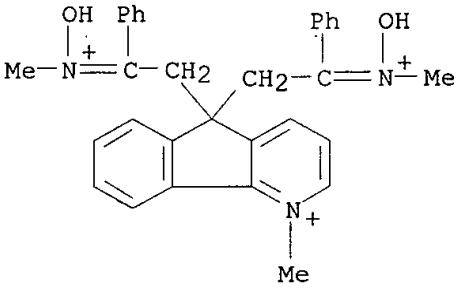
SR CA
LC STN Files: CA, CAPLUS



● 3 I^-

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 121:255618

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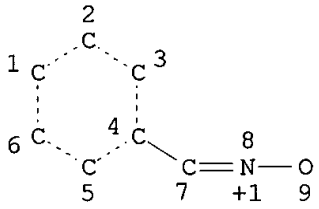

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CHARGE IS E+1 AT 8
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L3 63 SEA FILE=REGISTRY SSS FUL L1
L80 STR

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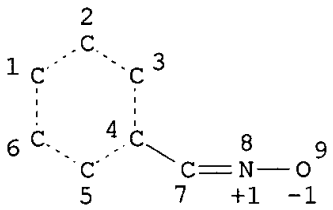

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CHARGE IS E-1 AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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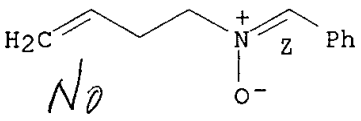
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L81 2 SEA FILE=REGISTRY SUB=L3 SSS FUL L80

100.0% PROCESSED 63 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L81 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 23010-80-2 REGISTRY
CN Nitrone, N-3-butenyl-.alpha.-phenyl-, (Z)- (8CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H13 N O
LC STN Files: CA, CAPLUS

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 71:38845 exo-2-Phenyl-1-aza-7-oxabicyclo[2.2.1]heptane, a novel heterobicyclic ring system. Lumma, William C., Jr. (Saint Louis Univ., Saint Louis, Mo., USA). J. Amer. Chem. Soc., 91(10), 2820-1 (English) 1969. CODEN: JACSAT.
GI For diagram(s), see printed CA Issue.
AB exo-2-Phenyl-1-aza-7-oxabicyclo-[2.2.1]heptane (I) was synthesized by intramol. 4 + 2 cycloaddn. of a nitrone to a double bond. Slow fractional distn., or refluxing in xylene for 24 hrs. of N-1-buten-3-yl-anti-benzaldoxime (II) gave a basic product from which was isolated a cryst. picrate. Treatment of the picrate with aq. Na2CO3 gave an isomer of II which was identified as I by ir and N.M.R. spectroscopy and chem. anal. Hydrogenolysis followed by methylation with HCHO and HCO2H produced

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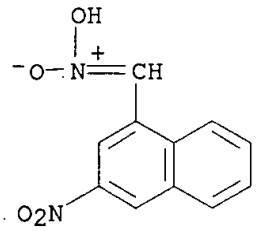
cis-1-methyl-2-phenyl-4-piperidinol. Possible reaction mechanisms are discussed.

L81 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 1506-03-2 REGISTRY
CN Naphthalene, 3-nitro-1-(aci-nitromethyl)- (7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C11 H8 N2 O4
LC STN Files: CA, CAOLD, CAPLUS



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 62:90690 Reactions of 2,3-dinitronaphthalene with carbanions and products resulting therefrom. Morrison, Donald C. (Fundamental Research Co.). US 3177241 19650406, 4 pp. (Unavailable). APPLICATION: US 19611005.
GI For diagram(s), see printed CA Issue.
AB Reaction of 5 g. Na with 350 g. MeOH was followed by addn. of 35 g. AcCH2CO2Et and then 32 g. 2,3-dinitronaphthalene (I). The mixt. was refluxed 45 min., cooled, and dild. with H2O to give 85.8% II (R : CH2CO2Me). Sapon. of the latter compd. gave 90.7% II (R : CH2CO2H), which heated with AmONO gave II (R : CN). Use of EtOH in the first reaction in place of MeOH gave 93% II (R : CH2CO2Et). Use of (EtO2C)2CH2 in place of the ester in the latter reaction gave 92.5% of the same product. Reaction of I with Na salt of di-Et oxalacetate in MeOH gave II (R : CH2CO2Me). Use of MeNO2 in the first reaction in place of the ester gave 74% of a mixt. of II (R : CH2N2) and II [R : CH-(:NO)OH.]. Use of EtNO2 in place of MeNO2 in the latter reaction gave 79% II (R : CHMeNO2), and with PrNO2 gave II (R CHEtNO2). Reaction of I with NaOMe and cyclopentadiene gave II (R : cyclopentadienyl), with indene gave 3-nitro-1-(1-naphthyl)indene, and with NCCH2CO2Et gave II [R : CH(CN)CO2Me]. KOH in MeOH with AcCH2CO2Me and I gave 87.8% II (R : CH2CO2Me). The first reaction is postulated to occur via initial reaction to give II [R : CHAcCO2Et), followed by alk. cleavage to give II (R : CH2CO2Et), followed by transesterification to give the observed product.

=> s ?nitrone?/cns
L82 1107 ?NITRONE?/CNS

=> d l84 que stat;s l84 or l84
L83 STR

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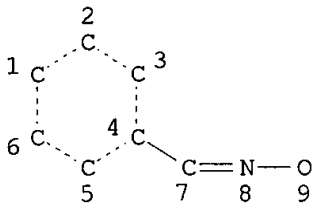

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L84 61744 SEA FILE=REGISTRY SSS FUL L83

100.0% PROCESSED 71420 ITERATIONS 61744 ANSWERS
SEARCH TIME: 00.00.01

L85 61744 L84 OR L84

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9000 RN 305811-23-8 REGISTRY
18000 RN 197299-36-8 REGISTRY
27000 RN 162216-54-8 REGISTRY
36000 RN 133408-72-7 REGISTRY
45000 RN 93183-03-0 REGISTRY
54000 RN 58041-17-1 REGISTRY

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L86 9000 L84 OR L84

=> s l85 range=(197299-36-8,305811-23-8)
L87 9001 L84 OR L84

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L90 9001 L84 OR L84

=> s l85 range=(58041-17-1,93183-03-0)
L91 9001 L84 OR L84

=> s l85 range=(,58041-17-1)
L92 7745 L84 OR L84

=> fil medl,hcap,biosis,jicst,embase;s (l86 or l87 or l88 or l89 or l90 or l91 or l92)

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       192.27     609.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -1.18     -12.33

FILE 'MEDLINE' ENTERED AT 07:54:57 ON 10 DEC 2002

FILE 'HCAPLUS' ENTERED AT 07:54:57 ON 10 DEC 2002
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FILE 'JICST-EPLUS' ENTERED AT 07:54:57 ON 10 DEC 2002
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THE ESTIMATED SEARCH COST FOR FILE 'MEDLINE' IS 1,235.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
L93        1363 FILE MEDLINE
L94       18351 FILE HCAPLUS
THE ESTIMATED SEARCH COST FOR FILE 'BIOSIS' IS 1,235.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
L95        2489 FILE BIOSIS
THE ESTIMATED SEARCH COST FOR FILE 'JICST-EPLUS' IS 1,235.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
L96           0 FILE JICST-EPLUS
THE ESTIMATED SEARCH COST FOR FILE 'EMBASE' IS 1,235.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
L97        5857 FILE EMBASE

TOTAL FOR ALL FILES
L98       28060 (L86 OR L87 OR L88 OR L89 OR L90 OR L91 OR L92)

=> s l98 and (neurodegener? or autoimmun? or inflamm? or neurolog? or immun?)
L99           73 FILE MEDLINE
L100         766 FILE HCAPLUS
L101         345 FILE BIOSIS
L102           0 FILE JICST-EPLUS
L103         297 FILE EMBASE

TOTAL FOR ALL FILES
L104        1481 L98 AND (NEURODEGENER? OR AUTOIMMUN? OR INFLAMM? OR NEUROLOG?
                 OR IMMUN?)

=> s l98 and (automimmun?(a)(disease or disorder) or autoimmunity or autoantibod?
or lupus or ms or multiple sclerosis or arthritis or purpura or reiter or
thyroiditis or grave? or addison?)
L105          11 FILE MEDLINE
L106         211 FILE HCAPLUS
L107          19 FILE BIOSIS
L108           0 FILE JICST-EPLUS


Searched by: Mary Hale 308-4258 CM-1 1E01
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L109         61 FILE EMBASE

TOTAL FOR ALL FILES
L110        302 L98 AND (AUTOMIMMUN?(A)(DISEASE OR DISORDER) OR AUTOIMMUNITY OR
                AUTOANTIBOD? OR LUPUS OR MS OR MULTIPLE SCLEROSIS OR ARTHRITIS
                OR PURPURA OR REITER OR THYROIDITIS OR GRAVE? OR ADDISON?)

=>

=> s (l104 or l110) and (alzheimer? or parkinson? or hiv dementia or human
immunodeficiency virus dementia)
L111          2 FILE MEDLINE
L112         43 FILE HCAPLUS
L113         10 FILE BIOSIS
L114          0 FILE JICST-EPLUS
L115         22 FILE EMBASE

TOTAL FOR ALL FILES
L116         77 (L104 OR L110) AND (ALZHEIMER? OR PARKINSON? OR HIV DEMENTIA OR
                HUMAN IMMUNODEFICIENCY VIRUS DEMENTIA)

=> s l116 not (l72 or l54)
L117          2 FILE MEDLINE
L118         43 FILE HCAPLUS
L119         10 FILE BIOSIS
L120          0 FILE JICST-EPLUS
L121         22 FILE EMBASE

TOTAL FOR ALL FILES
L122         77 L116 NOT (L72 OR L54)

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PROCESSING COMPLETED FOR L122
L123         70 DUP REM L122 (7 DUPLICATES REMOVED)

=> d cbib abs 1-70

L123 ANSWER 1 OF 70  HCAPLUS  COPYRIGHT 2002 ACS
2002:868937   Document No. 137:353046  Preparation of azaheterocyclylmethyl
     derivatives of 7,8-dihydro-1,6,9-trioxa-3-aza-cyclopenta[a]naphthalene as
     5-HT1A antagonists.  Stack, Gary Paul; Tran, Megan (Wyeth, John, and
     Brother Ltd., USA).  PCT Int. Appl. WO 2002090362 A1 20021114, 39 pp.
     DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,
     CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,
     GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
     LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,
     RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU,
     ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF,
     CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,
     MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.
     APPLICATION: WO 2002-US14211 20020506.  PRIORITY: US 2001-PV289168
     20010507.
GI
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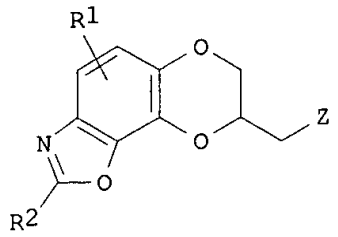
Searched by: Mary Hale 308-4258 CM-1 1E01



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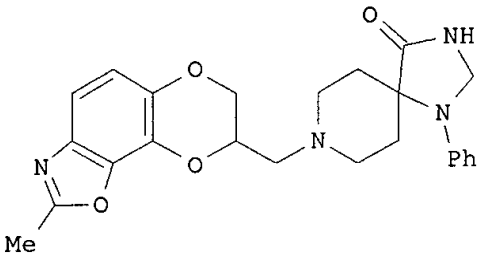

II

AB The title compds. [I; R1 = H, halo, CN, etc.; R2 = H, halo, CF3, etc.; Z = (un)substituted pyrrolidino, piperidino, etc.], useful for treating the cognitive deficits due to aging, stroke, head trauma, **Alzheimer**'s disease or other **neurodegenerative** diseases, or schizophrenia, were prepd. Thus, reacting (8R)-7,8-dihydro[1,4]dioxino[2,3-g][1,3]benzoxazol-8-ylmethyl 4-methylbenzenesulfonate (12-step synthesis given) with 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one in DMSO afforded (S)-II which showed Ki of 0.93 nM in test for 5-HT1A receptor affinity. The compds.I are also useful for the treatment of disorders such as anxiety, aggression and stress, and for the control of various physiol. phenomena, such as appetite, thermoregulation, sleep and sexual behavior.

L123 ANSWER 2 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:849646 Document No. 137:353043 Preparation of azabicyclylmethyl derivatives of 7,8-dihydro-1,6,9-trioxa-3-azacyclopenta[a]naphthalene as 5-HT1A antagonists. Stack, Gary Paul; Gilbert, Adam Matthew; Tran, Megan (Wyeth, John, and Brother Ltd., USA). PCT Int. Appl. WO 2002088145 A1 20021107, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13114 20020425. PRIORITY: US 2001-PV286818 20010426.

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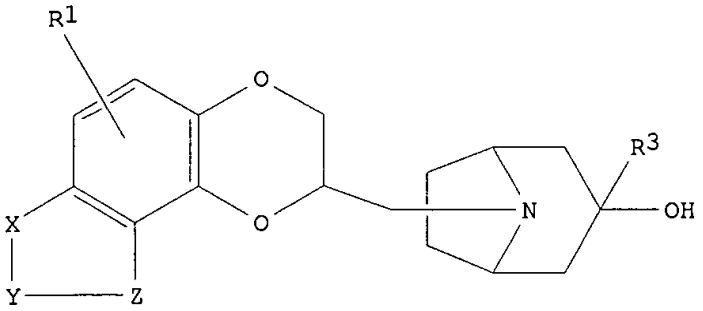

I

AB Azabicyclylmethyl derivs. of 7,8-dihydro-1,6,9-trioxa-3-azacyclopenta[a]naphthalene [I; wherein X-Y-Z = N:C(R2)-O, N:C(R2)-NH, NH-C(R2):CH; R1 = H, halo, CN, carboxamido, carboalkoxy, CF3, etc.; R2 = H, halo, CF3, amino, mono- or dialkylamino, etc.; R3 = Ph, naphthyl, anthracyl, phenanthryl, pyridyl, pyrimidyl, etc.] were prepd. For example, (8R)-2-methyl-7,8-dihydro[1,4]dioxino[2,3-g][1,3]benzoxazol-8-ylmethyl 4-methylbenzenesulfonate (synthetic prepn. given) was reacted with 3-phenyl-8-azabicyclo[3.2.1]octan-3-ol to give 8-{[2-methyl-7,8-dihydro[1,4]dioxino[2,3-g][1,3]benzoxazol-8-yl]methyl}-3-phenyl-8-azabicyclo[3.2.1]octanol. The title compds. are useful for treating the cognitive deficits due to aging, stroke, head trauma, **Alzheimer**'s disease or other **neurodegenerative** diseases, or schizophrenia and are also useful for the treatment of disorders such as anxiety, aggression and stress, and for the control of various physiol. phenomena, such as eating disorders, disorders of thermoregulation, and sleep and sexual dysfunction.

L123 ANSWER 3 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:849633 Document No. 137:353033 Preparation of azabicyclylmethyl derivatives of 2,3-dihydro-1,4-dioxino-[2,3-f]quinoline as 5-HT1A antagonists. Stack, Gary Paul; Gilbert, Adam Matthew; Tran, Megan (Wyeth, John, and Brother Ltd., USA). PCT Int. Appl. WO 2002088130 A1 20021107, 36 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US12953 20020425. PRIORITY: US 2001-PV286576 20010426.

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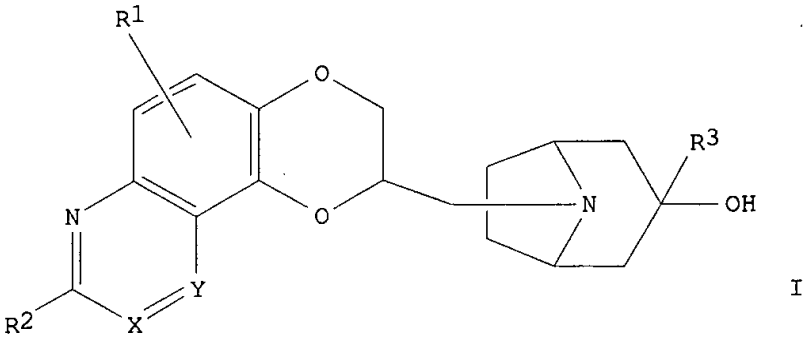
Searched by: Mary Hale 308-4258 CM-1 1E01



I

AB Azabicyclylmethyl derivs. of 2,3-dihydro-1,4-dioxino-[2,3-f]quinoline [I; wherein X = N, CR4; Y = N, CH; R1 = H, halo, CN, carboxamido, carboalkoxy, CF3, etc.; R2 = H, OH, halo, amino, mono- or dialkylamino, etc.; R3 = Ph, naphthyl, anthracyl, phenanthryl, pyridyl, pyrimidyl, etc.; R4 = H, (C1-C6)alkyl] were prepd. For example, (2R)-8-methyl-2,3-dihydro[1,4]dioxino[2,3-f]quinolin-2-ylmethyl 4-methylbenzenesulfonate (synthetic prepn. given) is reacted with 3-phenyl-8-aza-bicyclo[3.2.1]octan-3-ol to give the S-enantiomer of 8-{[8-methyl-2,3-dihydro[1,4]dioxino[2,3-f]quinolin-2-yl]methyl}-3-phenyl-8-azabicyclo[3.2.1]octan-3-ol. The title compds. are useful for treating the cognitive deficits due to aging, stroke, head trauma, **Alzheimer**'s disease or other **neurodegenerative** diseases, or schizophrenia and are also useful for the treatment of disorders such as anxiety, aggression and stress, and for the control of various physiol. phenomena, such as eating disorders, disorders of thermoregulation, and sleep and sexual dysfunction.

L123 ANSWER 4 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:814125 Document No. 137:325438 Preparation of dihydro-benzo[b][1,4]diazepin-2-one derivatives as metabotropic glutamate receptor 2 (mGluR2) antagonists. Adam, Geo; Goetschi, Erwin; Mutel, Vincent; Wichmann, Juergen; Woltering, Thomas Johannes (F. Hoffmann-La Roche AG, Switz.). PCT Int. Appl. WO 2002083665 A1 20021024, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP3643 20020402. PRIORITY: EP 2001-109126 20010412.

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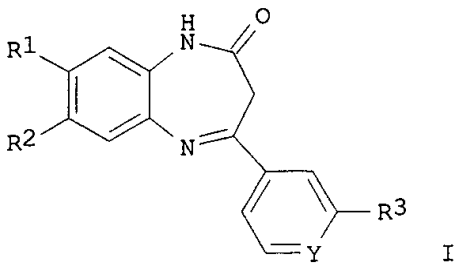
Searched by: Mary Hale 308-4258 CM-1 1E01



I

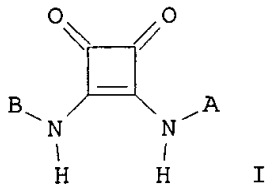
AB This invention is concerned with dihydro-benzo[b][1,4]diazepin-2-one derivs. of general formula [I; R1 = cyano, each (un)substituted fluoro-lower alkyl, lower alkoxy, fluoro-lower alkoxy, or is pyrrol-1-yl; R2 = H, if R1 is optionally substituted pyrrol-1-yl as defined above, or R2 = halogen, HO, lower alkyl, fluoro-lower alkyl, lower alkoxy, hydroxymethyl, hydroxyethoxy, lower alkoxy(ethoxy)n (n = 1-4), lower alkoxymethyl, cyanomethoxy, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, 4-oxopiperidin-1-yl 4-alkoxypiperidin-1-yl, 4-hydroxypiperidin-1-yl, 4-hydroxyethoxypiperidin-1-yl, 4-lower alkylpiperazin-1-yl, alkoxycarbonyl, 2-dialkylaminoethylsulfanyl, N,N-bis(lower alkyl)amino-lower alkyl, carbamoylmethyl, etc.; Y = CH, N; R3 = halogen, lower alkyl, fluoro-lower alkyl, lower alkoxy, cyano, -(CH2)nCO-OR''-(CH2)n-CO-NR'R'', or (un)substituted five-membered arom. heterocycle; R' = H, lower alkyl, C3-6-cycloalkyl, fluoro-lower alkyl or 2-lower alkoxy-lower alkyl; R" = H, lower alkyl, C3-6-cycloalkyl, fluoro-lower alkyl, 2-lower alkoxy lower alkyl, -(CH2)2-4-di-lower alkylamino, -(CH2)2-4-morpholinyl, -(CH2)2-4-pyrrolidinyl, -(CH2)2-4-piperidinyl, 3-hydroxy-lower alkyl; n = 0-4] and their pharmaceutically acceptable addn. salts. The invention further relates to medicaments contg. these compds. and a process for their prepn. as well as their use for prepn. of medicaments for the treatment or prevention of acute and/or chronic **neurol**. disorders including psychosis, schizophrenia, **Alzheimer**'s disease, cognitive disorders and memory deficits. Thus, a mixt. of (2-amino-5-thiomorpholin-4-yl-4-trifluoromethylphenyl)carbamic acid tert-Bu ester and 3-(2-cyanopyridin-4-yl)-3-oxopropionic acid tert-Bu ester in toluene was heated to 80-120.degree. to give [2-[3-(2-cyanopyridin-4-yl)-3-oxopropionylamino]-5-thiomorpholin-4-yl-4-trifluoromethylphenyl]carbamic acid tert-Bu ester which was treated with CF3CO2H in CH2Cl2 to give 4-(4-Oxo-8-thiomorpholin-4-yl-7-trifluoromethyl-4,5-dihydro-3H-benzo[b][1,4]diazepin-2-yl)pyridine-2-carbonitrile (II). II in vitro inhibited the [3H]-LY354740 binding on mGluR2 transfected CHO cell membranes with Ki of 0.0009 .mu.M.

L123 ANSWER 5 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:814089 Document No. 137:325178 Preparation of 3,4-di-substituted cyclobutene-1,2-diones as cxc-chemokine receptor ligands. Taveras, Arthur G.; Aki, Cynthia J.; Bond, Richard W.; Chao, Jianping; Dwyer, Michael; Ferreira, Johan A.; Chao, Jianhua; Yu, Younong; Baldwin, John J.; Kaiser, Bernd; Li, Ge; Merritt, J. Robert; Nelson, Kingsley H.; Rokosz, Laura L. (Schering Corporation, USA; Pharmacopeia, Inc.). PCT Int. Appl. WO 2002083624 A1 20021024, 394 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH,

CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US12681 20020415. PRIORITY: US 2001-PV284026 20010416.

GI



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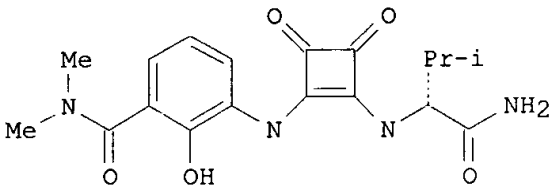

II

AB Title compds. I [A = (un)substituted heterocycle, heterocyclealkyl, heteroaryl, heteroarylalkyl, cycloalkyl, etc.; B = (un)substituted aryl, heteroaryl, heterocycle, heteroarylarene, etc.], or a pharmaceutically acceptable salt or solvate thereof, are prepd. and disclosed as cxc-chemokine receptor ligands. Thus, II was prepd. by substitution of (dimethylaminocarbonylhydroxyphenylamino)(ethoxy)cyclobutenedione [prepn. given] with (R)-2-amino-N,3-dimethylbutanamide monohydrochloride [prepn. given]. Compds. of the invention demonstrated an IC50 value of < 20 .mu.M in CXCR1 SPA assay and < 5 .mu.M in CXCR2 SPA assay. I are useful for the treatment of chemokine-mediated diseases such as acute and chronic **inflammatory** disorders and cancer.

L123 ANSWER 6 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2002:754196 Document No. 137:257677 Methods of treating or preventing **Alzheimer**'s disease using 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes. Nieman, James A.; Fang, Lawrence; Jagodzinska, Barbara (Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company). PCT Int. Appl. WO 2002076440 A2 20021003, 449 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9100 20020321. PRIORITY: US 2001-PV278371 20010323; US 2001-PV308729 20010730.

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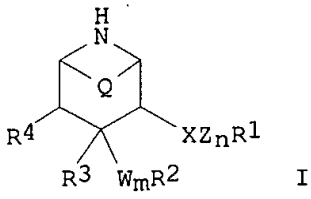

I

AB Disclosed are methods for treating or preventing **Alzheimer**'s disease, and other diseases, and/or inhibiting .beta.-secretase enzyme, and/or inhibiting deposition of A beta peptide in a mammal, using 3,4-disubstituted piperidinyl compds. (I) wherein the variables R1, R2, R3, R4, Q, W, X, Z, m, and n are defined below. Although neither the compds. nor the methods of prepn. are claimed, .apprx.150 example prepns., translations from the German examples of patent WO 9709311, are included. I inhibit .beta.-secretase with IC50 < 50 .mu.M; compds. that are effective inhibitors of .beta.-secretase activity demonstrate reduced cleavage of the substrate as compared to a control. In I, R1 is aryl, heterocycle; R2 is Ph, naphthyl, acenaphthyl, cyclohexyl, pyridyl, pyrimidinyl, pyrazinyl, oxopyridinyl, diazinyl, triazolyl, thienyl, oxazolyl, oxadiazolyl, thiazolyl, pyrrolyl, or furyl, optionally substituted. R3 is: H, hydroxy, lower-alkoxy, or lower-alkenyloxy; R4 is: H, lower-alkyl, lower-alkenyl, lower-alkoxy, hydroxy-lower-alkyl, lower-alkoxy-lower-alkyl, benzyl, oxo, or where R3 and R4 together are a bond, or as specified in the claims. Q is: ethylene, or is absent; X is: a bond, -O-, -S-, -CH-R11- (R11 defined in claims), -CHOR9- (R9 defined in claims), -OCO, -CO-, or C:NOR10- (R10 is carboxyalkyl, alkoxycarbonylalkyl, alkyl or H), with the bond emanating from an O or S atom joining to a satd. C atom of group Z or to R1; W is: -O-, or -S-; Z is: lower-alkylene, lower-alkenylene, hydroxy-lower-alkylidene, -O-, -S-, -O-Alk- (Alk is a lower alkylene), -S-Alk-, -Alk-O-, or -Alk-S. N is: 1, or 0 or 1 when X is -O-CO; and where m is 0 or 1; with provisos.

L123 ANSWER 7 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2002:736244 Document No. 137:247602 Preparation of (pyrrolidinylalkyl)benzofurans and analogs as histamine-3 receptor ligands for treatment of disorders related to CNS neurotransmission. Cowart, Marlon D.; Bennani, Youssef L.; Faghih, Ramin; Gfesser, Gregory A.; Black, Lawrence A. (Abbott Laboratories, USA). PCT Int. Appl. WO 2002074758 A2 20020926, 268 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US7107 20020311. PRIORITY: US 2001-810648 20010316; US 2002-44495 20020111; US 2002-81207 20020225.

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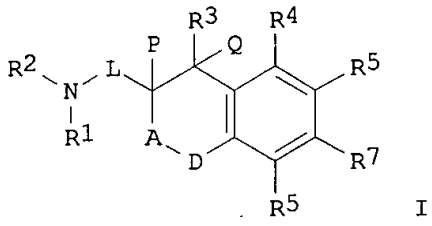

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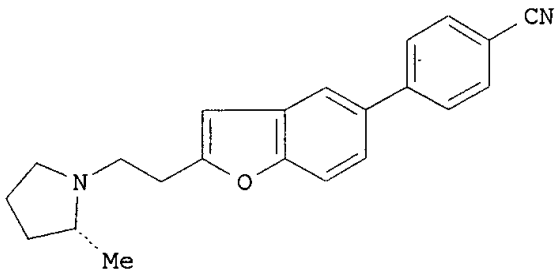

II

AB Title compds. I [wherein A = CO or covalent bond; D = O or S; L = alkylene, fluoroalkylene, or hydroxyalkylene; P and Q taken together form a covalent bond or are both H; R1 and R2 = independently H, (cyclo)alkyl, aryl(alkyl), cycloalkylalkyl, heterocyclyl(alkyl), hydroxyalkyl, alkenyl, or alkynyl; or NR1R2 = heterocyclyl; R3 = H, alkoxy(carbonyl), (halo)alkyl, alkylcarbonyl(oxy), alkylsufinyl, alkylsulfonyl, alkylthio, aryl, carboxy(alkyl), cyano(alkyl), formyl, halo(alkoxy), heterocyclyl, hydroxy(alkyl), SH, NO2, or (un)substituted amino(alkyl), carbamoyl, or sulfamoyl; R4-R7 = independently R3 or L2R20 or R20L3R22; L2 = alkylene, alkenylene, O, S, SO, SO2, CO, C:NOR21, or (un)substituted amino; L3 = covalent bond, alkylene, alkenylene, O, S, CO, N:OR21, or (un)substituted amino; R20 and R22 = independently aryl, heterocyclyl, or cycloalkyl; R21 = H or alkyl; or pharmaceutically acceptable salts, esters, amides, or prodrugs thereof] where prepd. for modulation of the histamine-3 (H3) receptors. For example, 4-hydroxy-4'-cyanobiphenyl was treated with NaI, NaOH, and NaOCl in MeOH to give 4'-hydroxy-3'-iodo-[1,1'-biphenyl]-4-carbonitrile (53%). Cyclization with 3-butyn-1-ol in DMF in the presence of CuI and Pd(PPh3)2Cl2 afforded 4-[2-(2-hydroxyethyl)-1-benzofuran-5-yl]benzonitrile (95%). Mesylation (89%), followed by addn. of (2R)-2-methylpyrrolidine.bul.HBr and Na2CO3 in AcCN (34%), produced II. The latter displayed binding activity to H3 receptors in rat brain cortex tissue with Ki of 4.44 nM. I are H3 receptor ligands that modulate function of the H3 receptor by antagonizing its activity. Thus, I are useful for the treatment of disorders ameliorated by H3 receptor ligands, esp. **Alzheimer**'s disease, attention-deficit hyperactivity disorder, epilepsy, narcolepsy, obesity, cognitive impairment, deficits of memory, deficits of learning, and dementia (no data).

L123 ANSWER 8 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2002:695727 Document No. 137:226646 Co-administration of melanocortin receptor agonist and phosphodiesterase inhibitor for treatment of cyclic-AMP associated disorders. Macor, John E.; Carlson, Kenneth E. (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2002069905 A2 20020912, 91 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,

OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US6805 20020304. PRIORITY: US 2001-PV273206 20010302; US 2001-PV273291 20010302; US 2001-PV289719 20010509.

AB Co-administration of a melanocortin receptor agonist, particularly an MC-1R or MC-4R agonist, and a cAMP phosphodiesterase inhibitor is described for modulating levels of cyclic adenosine 3',5' monophosphate (cAMP) in a mammal. The inventive co-administration is useful in the treatment of diseases affected by activity of cAMP-PDE, including without limitation, **inflammatory** bowel disease, irritable bowel syndrome, rheumatoid **arthritis**, osteoarthritis, pancreatitis, psoriasis, migraine, **Alzheimer**'s Disease, **Parkinson**'s disease, transplant rejection, asthma, acute respiratory distress syndrome, chronic obstructive pulmonary disease, stroke, and **neurodegeneration** of, and consequences of traumatic brain injury.

L123 ANSWER 9 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:594805 Document No. 137:154948 Preparation of N-(2-hydroxyphenylmethyl and 2-hydroxybenzylidene)hydrazine and -amine derivatives having Maillard reaction inhibitory activity. Tsutsumi, Seiji; Kawaguchi, Mami; Tadauchi, Kaori; Ninomiya, Tomohisa; Yahata, Naokazu; Nakatani, Yuko (Meiji Seika Kaisha, Ltd., Japan). PCT Int. Appl. WO 2002060858 A1 20020808, 193 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2002-JP786 20020131. PRIORITY: JP 2001-24414 20010131.

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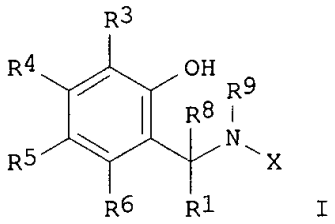

I

AB The title compds. represented by the formula (I) or pharmacol. acceptable salt thereof [R1 = (un)substituted alkyl, cycloalkyl, aryl, unsatd. heterocycle, satd. heterocycle, or phenylalkenyl; R3, R4, R5, R6 = H, OH, nitro, halogeno, alkyl, alkoxy, mercapto, alkylthio, amino, alkylamino, dialkylamino, or phenyl; R8 = hydrogen or a bond in cooperation with R9; R9 = H, alkyl, alkyl, alkoxy, alkanoyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl; X = NR7aCOR2a (wherein R2a = alkyl, etc.; R7a = hydrogen, alkyl, etc.), NR7bC(Y)R2b (wherein R2b = alkyl, etc.; Y = oxo, etc.), or (CH2)nCR11cR12cR2c (wherein R2c = unsatd. heterocycle, etc.; R11c, R12c = H, alkyl, etc.; n = an integer of 0 to 4)] and pharmacol. acceptable salts thereof having strong inhibitory activity against the Maillard reaction were prepd. Also disclosed are a medicine contg. I for use in the

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prevention of or treatments for diseases such as diabetic nephropathy, diabetic neuropathy, diabetic retinopathy, cataract, great vascular diseases, **Alzheimer**'s disease, amyotrophic lateral sclerosis, dialysis amyloidosis, or articular rheumatism which the Maillard reaction participates and an additive contg. I for preventing the deterioration of cosmetics or foods caused by the Maillard reaction. Thus, 2'-hydroxy-2-(4-methylpiperazin-1-yl)acetophenone was condensed with hydrazine hydrate in ethanol at room temp. for 30 min and acylated by 2-acetoxybenzoyl chloride in pyridine at room temp. for 30 min to give (Z)-2-acetoxybenzoic acid [1-(2-hydroxyphenyl)-2-[4-(2-methoxyphenyl)piperazin-1-yl]ethylidene]hydrazide. N,N-diethyl-(E)-3-[[[1-(2-hydroxy-5-methylphenyl)-2-phenylethylidene]hydrazino]carbonyl]benzenesulfonamide in vitro showed IC50 of 0.6 .mu.M for inhibiting the formation of advanced glycation end products (AGE) from lysozyme and fructose. A tablet and a granule formulation contg. (E)-2-hydroxybenzoic acid [1-(2-hydorxyphenuyl)-1-phenylmethylene]hydrazide were also prepd.

L123 ANSWER 10 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2002:275968 Document No. 136:309857 Preparation of quinolines and quinolinones as metabotropic glutamate receptor antagonists. Mabire, Dominique Jean-Pierre; Venet, Marc Gaston; Coupa, Sophie; Poncelet, Alain Philippe; Lesage, Anne Simone Josephine (Janssen Pharmaceutica N.V., Belg.). PCT Int. Appl. WO 2002028837 A1 20020411, 114 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP11135 20010925. PRIORITY: EP 2000-203419 20001002.

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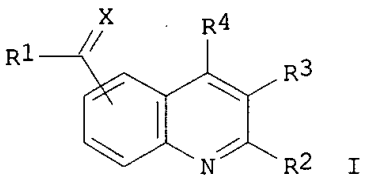

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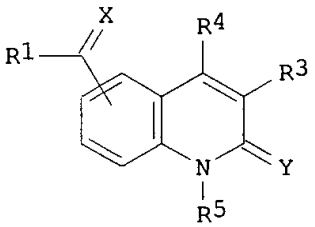

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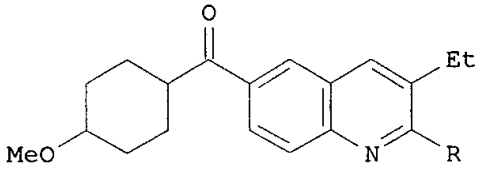

III

AB The title compds. [I or II; X = O, C(R6)2; (wherein R6 = H, aryl, alkyl, etc.); R1 = alkyl, aryl, thienyl, etc.; R2 = H, halo, CN, etc.; R3, R4 = H, alkyl; or R2 and R3 may be taken together to form (CH2)3, (CH2)4,

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CH:CHCH:CH, etc.; or R3 and R4 may be taken together to form CH:CHCH:CH, (CH2)4; R5 = H, cycloalkyl, piperidinyl, etc.; Y = O, S; or Y and R5 may be taken together to form CH:NN, N:NN, NCH:CH], useful for treating or preventing glutamate-induced diseases of the central nervous system, were prepd. Thus, reacting cis-III [R = Cl] with SnMe4 in the presence of Pg(PPh3)4 in PhMe afforded 17% cis-III [R = Me] which showed antagonism at a dose of 2.5 mg/kg bodyweight in cold allodynia test in rats with a Bennett ligation.

L123 ANSWER 11 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:142686 Document No. 136:200192 Preparation of heterocyclic compounds as PPAR (peroxisome proliferator activated receptor) .delta. activators. Sakuma, Shogo; Endo, Tsuyoshi; Tendo, Atsushi; Takahashi, Toshihiro; Yoshida, Shinichi; Kobayashi, Kunio; Mochiduki, Nobutaka; Yamakawa, Tomio; Kanda, Takashi; Masui, Seiichiro (Nippon Chemiphar Co., Ltd., Japan). PCT Int. Appl. WO 2002014291 A1 20020221, 92 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2001-JP6836 20010809. PRIORITY: JP 2000-243596 20000811; JP 2000-402893 20001228.

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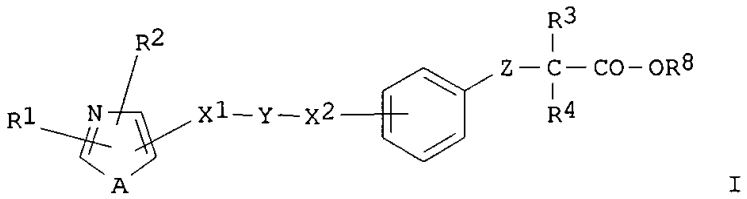

I

AB The title compds. I [R1 and R2 are each hydrogen, C1-8 alkyl, an aryl or heterocyclic group which may be substituted, or the like; A is oxygen, sulfur, or the like; X1 and X2 are each O, S(O)p (wherein p is an integer of 0 to 2), or the like; Y is optionally substituted C1-8 alkylene; Z is O or S ; R3 and R4 are each optionally substituted C1-8 alkyl; and R8 is hydrogen or C1-8 alkyl; a proviso is given] are prepd. The PPAR .delta. activating activity of 2-[4-[3-[2-(2,4-dichlorophenyl)-5-isopropyl-4-oxazolyl]propionyl]phenyloxy]-2-methylpropionic acid (II) is more potent than that shown by the known L-165041; II also showed high selectivity for the PPAR .delta. receptors.

L123 ANSWER 12 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:142506 Document No. 136:177977 Methods for treating **inflammatory** diseases using PPAR agonists. Pershadsingh, Harrihar A. (USA). PCT Int. Appl. WO 2002013812 A1 20020221, 42 pp. DESIGNATED STATES: W: AU, CA, MX, NZ, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US25668 20010816. PRIORITY: US 2000-PV225907 20000817; US 2000-PV230509 20000906.

AB The present invention describes methods for the use of PPAR ligands in the treatment **inflammatory** endocrine, dermatol., cardiovascular **immunol.**, **neurol.**, ophthalmic, neoplastic, pulmonary

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diseases, and age-related dysregulations. In addn., methods are provided for treating said conditions and diseases comprising the step of administering to a human or an animal in need thereof a therapeutic amt. of pharmacol. compns. comprising a pharmaceutically acceptable carrier, and a PPAR.gamma. agonist which cross-activates PPAR.alpha. or PPAR.delta. or both, or a PPAR.gamma. partial agonist, or a PPAR.gamma./RXR agonist, effective to reverse, slow, stop, or prevent the pathol. **inflammatory** or degenerative process.

L123 ANSWER 13 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2002:889587 Preparation of benzisoxazolyloxyacetic acids for treatment of diabetes and lipid disorders. Liu, Kun; Xu, Libo; Jones, A. Brian (USA). U.S. Pat. Appl. Publ. US 20020173663 A1 20021121, 26 pp., Cont.-in-part of U.S. Ser. No. 782,856, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2001-932834 20010817. PRIORITY: US 2000-PV183593 20000218; US 2001-782856 20010214.

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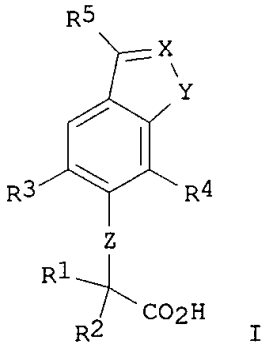

I

AB Title compds. [I; R1, R2 = H, F, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl; R1R2C = cycloalkyl; R3, R4 = alkyl, alkenyl, alkynyl, Cl; X = N, CR; Y = O, S, NR; Z = O, S; R = H, (substituted) alkyl, alkenyl, alkynyl; R5 = H, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryl, cycloalkyl, heteroaryl, etc.; with provisos], were prepd. as PPAR.alpha. and/or PPAR.gamma. agonists and are therefore useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus, hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, **inflammation**, etc. (no data). Thus, 5,7-dipropyl-6-OH-3-CF3-1,2-benzisoxazole (prepn. given) was stirred with Me .alpha.-bromoisobutyrate and Cs2CO3 in DMF for 7 days at 60.degree. to give Me 2-[(5,7-dipropyl-3-CF3-1,2-benzisoxazol-6-yl)oxy]-2-methylpropionate.

L123 ANSWER 14 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2002:833521 Document No. 137:337683 Preparation of benzenebutyric acids as inhibitors of matrix metalloproteinases. Purchase, Claude Forsey; Roth, Bruce David; White, Andrew David (Warner-Lambert Company, USA). U.S. Pat. Appl. Publ. US 2002161050 A1 20021031, 43 pp., Division of U. S. Ser. No. 351,549. (English). CODEN: USXXCO. APPLICATION: US 2001-23288 20011217. PRIORITY: US 1999-351549 19990712.

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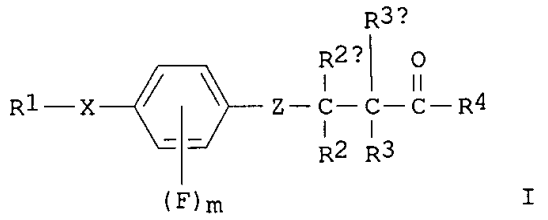
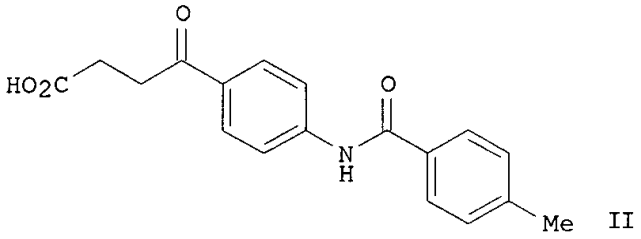


I



II

AB The title compds. with general formula of I [wherein R1 = H, (cyclo)alkyl, (hetero)aryl, (hetero)arylalkyl, or heterocyclyl(alkyl); R2, R2a, R3, and R3a = independently H, F, R5, NR7CO-alkyl, alkanoyl(oxy), alkoxycarbonyl, alkanoylthio, NR7-alkyl, alkylsulfinyl, alkylsulfonyl(amino), CN, CF3, or (un)substituted alkyl-R5; R5 = H, (hetero)aryl, heterocyclyl, N-naphthalimido, N-2,3-naphthylimido, indol-3-yl, imidazol-4-yl, pyridyl, 2,4-dioxo-1,5,5-trimethylimidazolidin-3-yl, or a side chain of an (un)naturally occurring amino acid; R4 = SH, OR4a, or NHOR4a; R4a = H, (aryl)alkyl, cycloalkyl, or aryloxymethyl; X = COCH2, CONR6, NR6CO, CO2, OCO, CO, CH(OH), C(=NH)NR6, OCO2, OCONR6, NR6CO2, NR6CONR6a, CSNR6, NR6CS, CSO, OCS, OCSO, OCSNR6, NR6CSO, or NR6CSNR6a; R6 and R6a = independently H or CH3; or R1 and R6 together form a ring contg. (un)substituted 4-7 carbons, etc.; Z = CO, CN(OR7), C(OH)R7, CHF, or CF2; R7 = H or alkyl; m = 0-4; or isomers and pharmaceutically acceptable salts thereof] where prepd. as inhibitors of matrix metalloproteinases (MMP), particularly gelatinase A, collagenase-3, and stromelysin-1. For example, reaction of acetanilide and succinic anhydride in DMF in the presence of AlCl3 gave 4-(4-acetylaminophenyl)-4-oxobutyric acid. The above compd. was treated with 1.0 M aq. HCl, followed by 50% wt./wt. aq. NaOH, and again by 1.0 M aq. HCl to give 4-(4-aminophenyl)-4-oxobutyric acid. Subsequent esterification, amidation, and hydrolysis of the above compd. afforded 4-[4-(4-methylbenzoylamino)phenyl]-4-oxobutyric acid (II). II showed the activity vs. MMP-2CD, MMP-3CD, and MMP-13CD with IC50 values of 0.22 .mu.M, 1.55 .mu.M, and 5.8 .mu.M, resp. I are useful for the treatment of **multiple sclerosis**, atherosclerotic plaque rupture, aortic aneurysm, heart failure, left ventricular dilation, restenosis, periodontal disease, corneal ulceration, treatment of burns, decubital ulcers, wound healing, cancer, **inflammation**, pain, **arthritis**, osteoporosis, renal disease, or other **autoimmune** or **inflammatory** disorders dependent upon tissue invasion by leukocytes or other activated migrating cells, acute and chronic **neurodegenerative** disorders including stroke, head trauma, spinal cord injury, **Alzheimer**'s disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, **Parkinson**'s disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy (no data).

L123 ANSWER 15 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2002266537 EMBASE Sertraline: A review of its use in the management of major depressive disorder in elderly patients. Muijsers R.B.R.; Plosker G.L.;

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Noble S.. R.B.R. Muijsers, Adis International Limited, 41 Centorian Drive, Mairangi Bay, Auckland 10, New Zealand. demail@adis.co.nz. Drugs and Aging 19/5 (377-392) 2002.
Refs: 68.
ISSN: 1170-229X. CODEN: DRAGE6. Pub. Country: New Zealand. Language: English. Summary Language: English.

AB Sertraline is a selective serotonin reuptake inhibitor (SSRI) with well established antidepressant and anxiolytic activity. Results from several well designed trials show that sertraline (50 to 200 mg/day) is effective in the treatment of major depressive disorder in elderly patients (.gtoreq.60 years of age). Primary endpoints in most studies included the Hamilton Depression Rating Scale (HDRS), Clinical Global Impression (CGI) score and the Montgomery-Asberg Depression Rating Scale (MADRS). Sertraline was significantly more effective than placebo, and was as effective as fluoxetine, nortriptyline and imipramine in elderly patients. During one trial, amitriptyline was significantly more effective than sertraline [mean reduction from baseline on one of six primary outcomes (HDRS)], although no quantitative data were provided. Subgroup analysis of data from a randomised, double-blind trial in elderly patients with major depressive disorder suggests that vascular morbidity, diabetes mellitus or **arthritis** does not affect the antidepressant effect of sertraline. Secondary endpoints from these clinical trials suggest that sertraline has significant benefits over nortriptyline in terms of quality of life. In addition, significant differences favouring sertraline in comparison with nortriptyline and fluoxetine have been recorded for a number of cognitive functioning parameters. Sertraline is generally well tolerated in elderly patients with major depressive disorder, and lacks the marked anticholinergic effects that characterise the adverse event profiles of tricyclic antidepressants (TCAs). The most frequently reported adverse events in patients aged .gtoreq.60 years with major depressive disorder receiving sertraline 50 to 150 mg/day were dry mouth, headache, diarrhoea, nausea, insomnia, somnolence, constipation, dizziness, sweating and taste abnormalities. The tolerability profile of sertraline is generally similar in younger and elderly patients. Sertraline has a low potential for drug interactions at the level of the cytochrome P450 enzyme system. In addition, no dosage adjustments are warranted for elderly patients solely based on age. Conclusion: Sertraline is an effective and well tolerated antidepressant for the treatment of major depressive disorder in patients aged .gtoreq.60 years. Since elderly patients are particularly prone to the anticholinergic effects of TCAs as a class, SSRIs such as sertraline are likely to be a better choice for the treatment of major depressive disorder in this age group. In addition, sertraline may have advantages over the SSRIs paroxetine, fluoxetine and fluvoxamine in elderly patients because of the drug's comparatively low potential for drug interactions, which is of importance in patient groups such as the elderly who are likely to receive more than one drug regimen.

L123 ANSWER 16 OF 70 MEDLINE DUPLICATE 1
2002400755 Document Number: 22088442. PubMed ID: 12093096. Protection of malonate-induced GABA but not dopamine loss by GABA transporter blockade in rat striatum. Zeevalk Gail D; Manzino Lawrence; Sonsalla Patricia K. (Department of Neurology, University of Medicine and Dentistry of New Jersey, Piscataway, New Jersey 08854, USA.) EXPERIMENTAL NEUROLOGY, (2002 Jul) 176 (1) 193-202. Journal code: 0370712. ISSN: 0014-4886. Pub. country: United States. Language: English.

AB Previous work has shown that overstimulation of GABA(A) receptors can potentiate neuronal cell damage during excitotoxic or metabolic stress in vitro and that GABA(A) antagonists or GABA transport blockers are neuroprotective under these situations. Malonate, a reversible succinate dehydrogenase/mitochondrial complex II inhibitor, is frequently used in

animals to model cell loss in **neurodegenerative** diseases such as **Parkinson**'s and Huntington's diseases. To determine if GABA transporter blockade during mitochondrial impairment can protect neurons in vivo as compared with in vitro studies, rats received a stereotaxic infusion of malonate (2 micromol) into the left striatum to induce a metabolic stress. The nonsubstrate GABA transport blocker, NO711 (20 nmol) was infused in some rats 30 min before and 3 h following malonate infusion. After 1 week, dopamine and GABA levels in the striata were measured. Malonate caused a significant loss of striatal dopamine and GABA. Blockade of the GABA transporter significantly attenuated GABA, but not dopamine loss. In contrast with several in vitro reports, GABA(A) receptors were not a downstream mediator of protection by NO711. Intrastriatal infusion of malonate (2 micromol) plus or minus the GABA(A) receptor agonist muscimol (1 micromol), the GABA(A) Cl- binding site antagonist picrotoxin (50 nmol) or the GABA(B) receptor antagonist saclofen (33 nmol) did not modify loss of striatal dopamine or GABA when examined 1 week following infusion. These data show that GABA transporter blockade during mitochondrial impairment in the striatum provides protection to GABAergic neurons. GABA transporter blockade, which is currently a pharmacological strategy for the treatment of epilepsy, may thus also be beneficial in the treatment of acute and chronic conditions involving energy inhibition such as stroke/ischemia or Huntington's disease. These findings also point to fundamental differences between immature and adult neurons in the downstream involvement of GABA receptors during metabolic insult.

L123 ANSWER 17 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2001:545660 Document No. 135:137528 Preparation of nitrogenous cyclic compounds and pharmaceutical compositions containing the same as calcium antagonists. Yamamoto, Noboru; Suzuki, Yuichi; Kimura, Manami; Niidom, Tetsuhiro; Iimura, Yoichi; Teramoto, Tetsuyuki; Kaneda, Yoshihisa; Kaneko, Toshihiko; Kurusu, Nobuyuki; Shinmyo, Daisuke; Youskawa, Yukie; Hatakeyama, Shinji (Eisai Co., Ltd., Japan). PCT Int. Appl. WO 2001053258 A1 20010726, 289 pp. DESIGNATED STATES: W: AU, BR, CA, CN, HU, IL, KR, MX, NO, NZ, RU, US, ZA; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2001-JP288 20010118. PRIORITY: JP 2000-12176 20000120.

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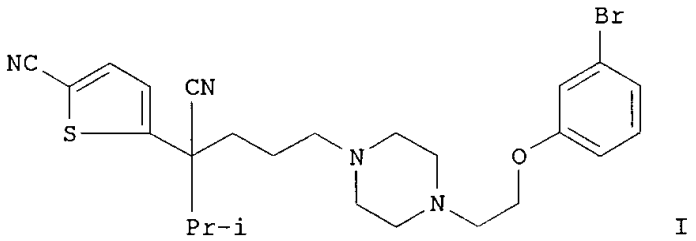

I

AB Title compds. [ArCR1(CN)D1ED2AW1XW2B; Ar is a group derived from an optionally substituted 5- to 14-membered arom. ring; ring A is one member selected from among piperazine, homopiperazine, and piperidine; ring B is an optionally substituted C3-14 hydrocarbon ring; E is a single bond, CO; R1 is hydrogen, halogeno, or hydroxyl; D1, D2, W1, W2 are each independently a single bond or optionally substituted C1-6 alkylene; X is a single bond, oxygen], salts, and hydrates are prepd. as calcium antagonists, particularly neuroselective calcium antagonists, and are used in pharmaceutical compns. Thus, title compd. I was prepd. and biol.

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tested for calcium antagonism.

L123 ANSWER 18 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2001:320074 Document No. 134:344595 Pharmaceutical compositions comprising primary N-hydroxylamines. Ames, Bruce N.; Atamna, Hani (The Regents of the University of California, USA). PCT Int. Appl. WO 2001030979 A1 20010503, 60 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US29634 20001027. PRIORITY: US 1999-429412 19991028.

AB The invention provides pharmaceutical compns. comprising primary N-hydroxylamines and related therapeutic, prophylactic, diagnostic and screening methods. The pharmaceutical compns. generally comprise a pharmaceutical compn. comprising an orally administrable effective unit solid dosage of a primary N-hydroxylamine or a pharmaceutically acceptable salt thereof and substantially free of a nitrone corresponding to the hydroxylamine. The compns. are useful for reducing oxidative damage or delaying senescence. N-tert-butylhydroxylamine, a hydrolysis product of .alpha.-phenyl-N-tert-butylnitrone, delayed senescence in IMR90 human lung fibroblasts. Tablets, capsules, and other formulations of N-tert-butylhydroxylamine are given.

L123 ANSWER 19 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2001:137022 Document No. 134:193431 3(5)-Ureidopyrazole derivatives, processes for their preparation and their therapeutic uses including antitumor agents. Pevarello, Paolo; Orsini,. Paolo; Traquandi, Gabriella; Varasi, Mario; Fritzen, Edward L.; Warpehoski, Martha A.; Pierce, Betsy S. (Pharmacia & Upjohn S.p.A., Italy; Pharmacia & Upjohn Company). PCT Int. Appl. WO 2001012188 A1 20010222, 54 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US17878 20000811. PRIORITY: US 1999-372833 19990812.

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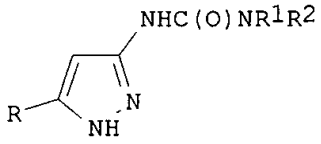

I

AB Compds. which are 3(5)-ureidopyrazole derivs. (I; e.g. N-(5-cyclopropyl-1H-pyrazol-3-yl)-N'-[2-(1-piperidinyl)ethyl]urea) or a pharmaceutically acceptable salt thereof, processes for their prepn. and their use as antitumor agents are claimed. In I: R = C1-C6 alkyl, aryl or arylalkyl group, which is optionally substituted with .gtoreq.1 OH, halogen, nitro, cyano, oxo, carboxy, amino, alkylamino, dialkylamino, alkylcarbonylamino, alkoxycarbonylamino, alkoxycarbonylalkylamino, aminocarbonylalkylamino, N-alkyl-N-carbonylamino, N-cycloalkyl-N-alkylaminoalkyl, aminoalkyl, aminocarbonyl, alkyl, cycloalkyl, alkylthio, alkoxy, alkylcarbonyl, alkylsulfonyl, alkylsulfonylamino, aminosulfonyl, alkoxycarbonyl, aryl, arylalkyl, aryloxy, arylthio, arylsulfonyl,

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arylamino, arylcarbonyl, N-alkylpiperazinyl, 4-morpholinyl, perfluorinated C1-C4 alkyl, C2-C4 alkenyl, C2-C4 alkynyl, C2-C4 aminoalkynyl or C2-C4 hydroxyalkynyl substituents. R1 = -(CH2)n-R3. N = 0-4. R3 = H, OH, amino, cycloalkyl, aryl and heterocyclyl, which is optionally substituted with .gtoreq.1 OH, halogen, nitro, cyano, oxo, carboxy, amino, alkylamino, dialkylamino, alkylcarbonylamino, alkoxycarbonylamino, alkoxycarbonylalkylamino, aminocarbonylalkylamino, N-alkyl-N-carbonylamino, N-cycloalkyl-N-alkylaminoalkyl, aminoalkyl, aminocarbonyl, alkyl, cycloalkyl, alkylthio, alkoxy, alkylcarbonyl, alkylsulfonyl, alkylsulfonylamino, aminosulfonyl, alkoxycarbonyl, aryl, arylalkyl, aryloxy, arylthio, arylsulfonyl, arylamino, arylcarbonyl, N-alkylpiperazinyl, 4-morpholinyl, perfluorinated C1-C4 alkyl, C2-C4 alkenyl, C2-C4 alkynyl, C2-C4 aminoalkynyl or C2-C4 hydroxyalkynyl substituents. R2 = H, or R2 and R1, together with the N atom to which they are bonded, form a heterocyclyl or heteroaryl group, which is optionally substituted with .gtoreq.1 OH, halogen, nitro, cyano, oxo, carboxy, amino, alkylamino, dialkylamino, alkylcarbonylamino, alkoxycarbonylamino, alkoxycarbonylalkylamino, aminocarbonylalkylamino, N-alkyl-N-carbonylamino, N-cycloalkyl-N-alkylaminoalkyl, aminoalkyl, aminocarbonyl, alkyl, cycloalkyl, alkylthio, alkoxy, alkylcarbonyl, alkylsulfonyl, alkylsulfonylamino, aminosulfonyl, alkoxycarbonyl, aryl, arylalkyl, aryloxy, arylthio, arylsulfonyl, arylamino, arylcarbonyl, N-alkylpiperazinyl, 4-morpholinyl, perfluorinated C1-C4 alkyl, C2-C4 alkenyl, C2-C4 alkynyl, C2-C4 aminoalkynyl or C2-C4 hydroxyalkynyl substituents. When n is 0 and R2 is H, R is a C3-C6 cycloalkyl group optionally substituted with a straight or branched C1-C6 alkyl group. The compds. are useful for the treatment of cancer, cell proliferative disorders, **Alzheimer**'s disease, viral infections, auto-**immune** diseases or **neurodegenerative** diseases, but no quant. test results are presented. The cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma. The cell proliferative disorder is selected from benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation assocd. with atherosclerosis, pulmonary fibrosis, **arthritis** glomerulonephritis and post-surgical stenosis and restenosis. The method of treatment provides tumor angiogenesis and metastasis inhibition, cell cycle inhibition or cdk/cyclin dependent inhibition, and treatment or prevention of radiotherapy-induced or chemotherapy-induced alopecia. A process for prepg. I comprises : (a) reacting a 3-amino-5-R-1H-pyrazole with a R1NCO to produce a 1-R1NHC(O)-3-R1NHC(O)NH-5-R-1H-pyrazole and (b) selectively hydrolyzing this intermediate in a basic medium to produce I. Another method comprises (c) reacting a 1-tert-butoxycarbonyl-3-amino-5-R-1H-pyrazole with 4-nitrophenyl chloroformate, or a polymer supported form of 4-nitrophenyl chloroformate, to produce a 1-tert-butoxycarbonyl-3-(4-nitrophenoxycarbonylamino)-5-R-1H-pyrazole, or a polymer supported form; (d) reacting this intermediate with a R1R2NH to produce a 1-tert-butoxycarbonyl-3-(R1R2NC(O)NH)-5-R-1H-pyrazole; (e) hydrolyzing this compd. in acidic medium to produce I; and, optionally, converting the 3-ureidopyrazole deriv. into another deriv., and/or into a salt thereof.

L123 ANSWER 20 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2001:392060 Document No. 135:511 Arylpiperidine and aryl-1,2,5,6-tetrahydropyridine urea derivatives. Kelly, Michael G.; Zhang, Gan (American Home Products Corporation, USA). U.S. US 6239126 B1 20010529, 9 pp. (English). CODEN: USXXAM. APPLICATION: US 1999-459791 19991213. PRIORITY: US 1998-PV150700 19981217.

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AB Compds. of the formula are useful for the treatment of disorder of the central nervous system including anxiety, depression, panic, alc. and drug addiction, sexual dysfunction, sleep disorders, migraine, obesity, cognitive disorders and **neurodegenerative** diseases. The compds. are shown to have high affinity for 5HT1A receptors and to have antagonist activity. The compds. can be used in combination with serotonin reuptake inhibitors.

L123 ANSWER 21 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2001:10087 Document No. 134:66173 Fluorine-substituted biphenyl butyric acids and their derivatives as inhibitors of matrix metalloproteinases. Purchase, Claude Forsey, Jr.; Roth, Bruce David; Schielke, Gerald Paul; Walker, Lary Craswell; White, Andrew David (Warner-Lambert, USA). U.S. US 6169103 B1 20010102, 31 pp. (English). CODEN: USXXAM. APPLICATION: US 1999-256714 19990224. PRIORITY: US 1998-PV76633 19980303.

AB Fluorine-substituted biphenyl butyric acid compds. and derivs. are described as well as acid methods for the prepn. and pharmaceutical compns. of same, which are useful as inhibitors of matrix metalloproteinases, particularly gelatinase A, stromelysin-1, and collagenase-3, and for the treatment of atherosclerotic plaque rupture, aortic aneurism, heart failure, restenosis, periodontal disease, corneal ulceration, treatment of burns, decubital ulcers, wound healing, cancer, **inflammation**, pain, **arthritis**, osteoporosis, **multiple sclerosis**, renal disease, and other **autoimmune** or **inflammatory** disorders dependent upon tissue invasion by leukocytes or other activated migrating cells, acute and chronic **neurodegenerative** disorders including stroke, head trauma, spinal cord injury, **Alzheimer**'s disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, **Parkinson**'s disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy.

L123 ANSWER 22 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001439851 EMBASE Dysregulation in neuroimmunopathology and perspectives of **immunotherapy**. Evseev V.A.; Davydova T.V.; Mikovskaya O.I.. V.A. Evseev, Laboratory of Neuroimmunopathology, Inst. Gen. Pathol./Pathol. Physiol., Russian Academy of Medical Sciences, Moscow, Russian Federation. Bulletin of Experimental Biology and Medicine 131/4 (305-308) 2001. Refs: 52.
ISSN: 0007-4888. CODEN: BEXBAN. Pub. Country: United States. Language: English. Summary Language: English.

AB Dysregulation of neuroimmune connections is a primary or secondary pathogenic factor of some CNS diseases. **Autoimmune** aggression is typical of **multiple sclerosis**, **Alzheimer**'s disease, and epilepsy, while dysregulation characterized by enhanced production of **autoantibodies** to neurotransmitters and activation of cell factors is characteristic of alcoholism and drug abuse. In experimental models of alcoholism and drug addiction, protective effects of antiserotonin antibodies are mediated by **immune** cells stimulated by these antibodies. These effects can be used in the therapy of various forms of neuroimmunopathology by the method of adoptive **immunotherapy**.

L123 ANSWER 23 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:432133 Document No.: PREV200100432133. SSRIs do not worsen **Parkinson**'s disease: Evidence from an open-label, prospective study. Dell'Agnello, Grazia; Ceravolo, Roberto; Nuti, Angelo; Bellini, Giovanna; Piccinni, Armando; D'Avino, Carla; Dell'Osso, Liliana; Bonuccelli, Ubaldo (1). (1) Department of Neuroscience, Clinical Neurology, University of Pisa, Via Roma 67, 56126, Pisa Italy. Clinical

Neuropharmacology, (July August, 2001) Vol. 24, No. 4, pp. 221-227. print.
ISSN: 0362-5664. Language: English. Summary Language: English.

AB Selective serotonin reuptake inhibitors (SSRIs) have been reported to be useful in the treatment of depression in patients with **Parkinson**'s disease (PD). However, a few reports have suggested that SSRIs may worsen **parkinsonian** motor symptomatology and extrapyramidal side effects have been reported in depressed patients treated with SSRIs. So far, no prospective trial comparing the effects of different SSRIs in depressed patients with PD has been performed. The aim of the present study was to assess the effects of four SSRIs (citalopram, fluoxetine, fluvoxamine, and sertraline) on motor performance and their efficacy on depression in a group of patients with PD. Sixty-two consecutive nondemented, nonfluctuating, depressed patients with PD were included in four treatment groups (15 patiens received citalopram, 16 fluoxetine, 16 fluvoxamine, and 15 sertraline). The evaluation of extrapyramidal and depressive symptomatology was performed with use of the Unified **Parkinson**'s Disease Rating Scale (UPDRS), Beck Depression Inventory, and Hamilton Depression Rating Scale at baseline and after 1, 3, and 6 months. Fifty-two patients completed the study. UPDRS scores were not significantly modified by the add-on therapy with each of the SSRIs studied. A significant improvement in depressive symptoms from baseline to the end of the trial was obtained with all SSRIs (Beck and Hamilton scores improving; $p<0.05$ according to an analysis of variance). Our findings suggest that SSRIs do not significantly worsen extrapyramidal symptomatology and may ameliorate depression in patients with PD.

L123 ANSWER 24 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2001214326 EMBASE Therapy and management of frontal lobe dementia patients.
Litvan I.. Dr. I. Litvan, Cognitive Neuropharmacology Unit, Henry M. Jackson Foundation, Champlain Building, 6410 Rockledge Drive, Bethesda, MD 20817-1844, United States. ilitvan@dvhip.org. Neurology 56/11 SUPPL. 4 (S41-S45) 2001.
Refs: 55.
ISSN: 0028-3878. CODEN: NEURAI. Pub. Country: United States. Language: English. Summary Language: English.

AB Patients with frontal lobe dementia (FLD) include those who suffer from Pick's disease, corticobasal degeneration, FLD without specific histopathologic features, as well as the infrequent families with frontotemporal dementia and **parkinsonism** associated with chromosome 17. Currently there have been no systematic efforts to manage and to treat patients with FLD. Drawing on the accumulated experience of clinicians and the known therapeutic approaches for patients with other **neurodegenerative** disorders such as AD and PD, the author discusses possible neurotransmitter replacement and biologic therapeutic approaches for patients with FLD.

L123 ANSWER 25 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2001167896 EMBASE Depression comorbid with anxiety or medical illness: The role of paroxetine. Rouillon F.. Prof. F. Rouillon, Hopital Albert Chenevier, 40 rue de Mesly, 94000 - Creteil, France. International Journal of Psychiatry in Clinical Practice 5/1 (3-10) 2001.
Refs: 83.
ISSN: 1365-1501. CODEN: IJPCFZ. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Depression is a common illness, frequently comorbid with other psychiatric disorders or medical illness. Comorbidity is associated with a poorer outcome for the patient, more severe symptoms and risk of suicide. The selective serotonin re-uptake inhibitor paroxetine has proven efficacy in the treatment of depression and anxiety disorders, including panic disorder, obsessive compulsive disorder and social anxiety disorder. The

paper examines the role of paroxetine monotherapy in the treatment of depressed patients with comorbid anxiety, and reviews the use of paroxetine in the treatment of depression in patients suffering concurrent medical illnesses.

L123 ANSWER 26 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2000:880948 Document No. 134:37041 Pharmaceutical compositions comprising iron chelators for the treatment of **neurodegenerative** disorders, some novel iron chelators, and compound preparation. Warshawsky, Abraham; Youdim, Moussa B. H.; Ben-Shachar, Dorit (Yeda Research and Development Co. Ltd., Israel; Technion Research and Development Foundation Ltd.). PCT Int. Appl. WO 2000074664 A2 20001214, 48 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-IL332 20000607. PRIORITY: IL 1999-130324 19990607.

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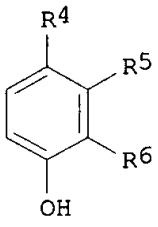

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AB The invention discloses the use of CH2[(R3CH2)2N]CH[N(CH2R3)2](CH2)nCONR1R 2 [R1 = H, hydrocarbyl; R2 = hydrophobic radical; R3 = 3-(C2-C6)acyl-4-hydroxyphenyl, 3-hydroxyimino(C2-C6)-alkyl-4-hydroxyphenyl, COOZ (Z = H, (C1-C6)alkyl, aryl or Ar(C1-C6)alkyl); n= 1-20], and of I [R4 = (C1-C6)acyl, nitro(C1-C6)alkyl, cyano(C1-C6)alkyl, (C1-C6)alkoxy(C1-C6)alkyl, CH2NR7R8; R7, R8, = H, (C1-C6)alkyl, or together with N atom form (un)satd. 5-7-membered ring optionally contg. further heteroatom selected from N, O or S, further N atom optionally substituted; either R5 = H and R6 = (C2-C6) acyl, hydroxyimino(C2-C6)alkyl, or R5 and R6 together with the Ph ring form a quinoline, a 1,2,3,4-tetrahydroquinoline or a perhydroquinoline ring], for the prepn. of pharmaceutical compns. for the treatment of **Parkinson**'s disease or stroke.

L123 ANSWER 27 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2000:725418 Document No. 133:296324 Synthesis and phosphodiesterase IV inhibition activity of purine derivatives. Chasin, Mark; Cavalla, David; Hofer, Peter; Gehrig, Andre; Wintergest, Peter (Euro-Celtique S.A., Luxembourg). PCT Int. Appl. WO 2000059449 A2 20001012, 112 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,

TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US8525 20000331. PRIORITY: US 1999-285473 19990402.

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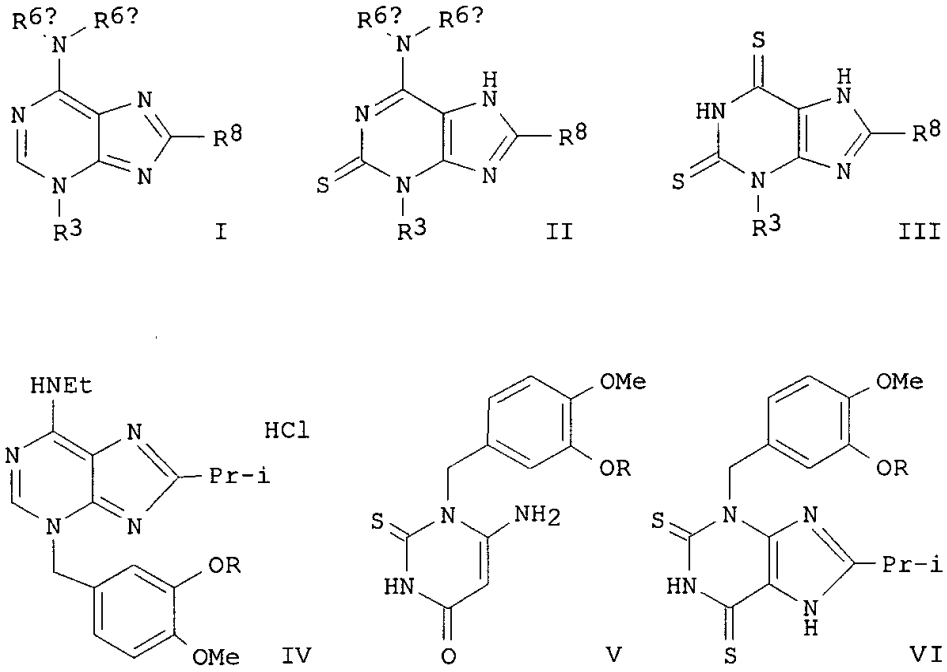

AB The purine (I) (R3, R8, R6a, R6b = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heterocyclyl, heteroaryl etc.), thioisoguanine (II), dithioxanthine (III) derivs., and their pharmaceutically accepted salts were synthesized. Thus, purine (IV; R = (CH2)5) was prepd. by etherification of isovanilline with cyclopentanol, oximation, redn. to amine, conversion to isothiocyanate, amination to thiourea followed by heterocyclization with Et cyanoacetate to thiouracil (V). V was nitrosylated, reduced, reacted with isobutyric anhydride to give isobutyrylamine which on treatment with phosphorus pentasulfide gave dithioxanthine (VI). VI, in a pressure reactor gave purine-2-thione which was reduced with Raney-nickel to give IV. The IC50 of IV against phosphodiesterase IV inhibition was 0.32 .mu.M. I, II and III were effective in effecting PDE IV inhibition in patients in need thereof.

L123 ANSWER 28 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2000:98541 Document No. 132:151674 Preparation of tricyclic heteroaromatics as inhibitors of matrix metalloproteinases. O'Brien, Patrick Michael; Picard, Joseph Armand; Sliskovic, Drago Robert (Warner-Lambert Company, USA). PCT Int. Appl. WO 2000006560 A1 20000210, 108 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN,

TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US12272 19990602. PRIORITY: US 1998-94705 19980730.

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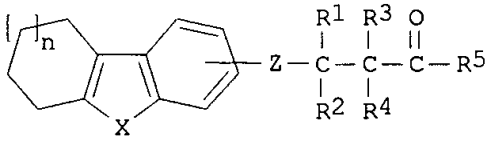

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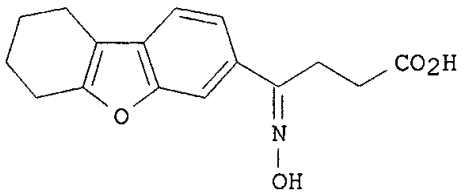

II

AB The title compds. [I; n = 1-2; X = O, CO, CH2, etc.; Z = CO, CHOH, CS, etc.; R1-R4 = H, F, alkyl, etc.; R5 = OH, SH, O(alkyl), etc.], useful as inhibitors of matrix metalloproteinases, particularly gelatinase A, collagenase-3, and stromelysin-1 and for the treatment of **multiple sclerosis**, atherosclerotic plaque rupture, aortic aneurysm, heart failure, left ventricular dilation, restenosis, periodontal disease, corneal ulceration, treatment of burns, decubital ulcers, wound healing, cancer, **inflammation**, pain, **arthritis**, osteoporosis, renal disease, or other **autoimmune** or **inflammatory** disorders dependent upon tissue invasion by leukocytes or other activated migrating cells, acute and chronic **neurodegenerative** disorders including stroke, head trauma, spinal cord injury, **Alzheimer**'s disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, **Parkinson**'s disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy, were prepd. Thus, treatment of 4-oxo-4-(6,7,8,9-tetrahydrodibenzofurn-3-yl)butyric acid with hydroxylamine hydrochloride in the presence of AcONa.3H2O in MeOH afforded 51% II which showed IC50 of 100 .mu.M against collagenase-1 full length enzyme.

L123 ANSWER 29 OF 70 HCAPLUS COPYRIGHT 2002 ACS

2002:781497 Document No. 137:262957 Preparation of aryloxyalkylamines as histamine H3 receptor modulators. Schwartz, Jean-Charles; Arrang, Jean-Michel; Garbarg, Monique; Lecomte, Jeanne-Marie; Ligneau, Xavier; Schunack, Walter G.; Stark, Holger; Ganellin, Charon Robin; Leurquin, Fabien; Sigurd, Elz (Societe Civile Bioprojet, Fr.). PCT Int. Appl. WO 2000006254 A2 20000210, 195 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP5744 19990729. PRIORITY: EP 1998-401944 19980729; EP 1998-403351 19981231.

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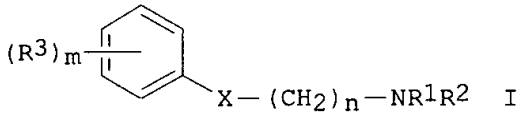

I

AB The title non-imidazole compds. I [wherein n = 2-8; m = 0-5; X = O, S; R1, R2 = alkyl, cycloalkyl; NR1R2 = (unsatd.) N-contg. ring, substituted piperazino; R3 = halo, alkyl, cycloalkyl, CF3, aryl, alkoxy, aryloxy, NO2, CHO, alkanoyl, aroyl, aralkanoyl, amino, carboxamido, cyano, alkoximino, alkenyl, alkynyl, etc.; and their pharmaceutically acceptable salts, hydrates, polymorphic cryst. structures,optical isomers, racemates, diastereoisomers, and enantiomers] were prepd. as antagonists and/or agonists of the histamine H3-receptors. Thus, 1-[3-(4-cyanophenoxy)prg167opyl]piperidine hydrogen oxalate (general prepn. given) increased telemethylhistamine in mice with ED50 = 0.20 mg/kg orally. I are useful for the treatment of central nervous system disorders, in particular **Alzheimer**'s disease, mood and attention alterations, cognitive deficits in psychiatric pathologies, obesity, vertigo, and motion sickness (no data).

L123 ANSWER 30 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2000:589999 Document No. 133:177185 Preparation of 1-N-alkyl-N-arylpyrimidinamines as CRF inhibitors. Aldrich, Paul Edward; Arvanitis, Argyrios Georgios; Bakthavatchalam, Rajagopal; Beck, James Peter; Cheeseman, Robert Scott; Chorvat, Robert John; Gilligan, Paul Joseph; Hodge, Carl Nicholas; Wasserman, Zelda Rakowitz (Dupont Pharmaceuticals Company, USA). U.S. US 6107301 A 20000822, 96 pp., Cont.-in-part of U.S. Ser. No. 315,660, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1997-906349 19970805. PRIORITY: US 1993-134209 19931012; US 1994-297274 19940826; US 1994-315660 19940929.

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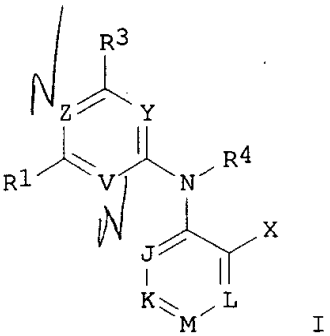

I

AB The title compds. [I; Y = CR29; R1 = alkyl, alkenyl, alkynyl, etc.; R3 = aryl, haloalkyl, (un)substituted NH2, etc.; J, K, L = CH, CX1; M = CR5; V = N; Z = N; R4 = H, halo, halomethyl, etc.; R4 is taken together with R29 to form a 5-membered ring and is N; X = Cl, Br, I, etc.; X1 = H, Cl, Br, etc.; R5 = halo, alkyl, haloalkyl, etc.] and their pharmaceutically acceptable salts, useful in the treatment of affective disorders, anxiety, depression, post-traumatic stress disorders, eating disorders, supranuclear palsy, irritable bowel syndrome, **immune**

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suppression, **Alzheimer**'s disease, gastrointestinal diseases, anorexia nervosa, drug and alc. withdrawal symptoms, drug addiction, **inflammatory** disorders, or fertility problems, were prepd. and formulated. E.g., a 3-step synthesis of I [Y = V = N; Z = CH; J, K, L = CH; M = C(Me); X = Br; R1, R3, R4 = Me] which showed Ki of 501-2000 nM against CRF receptor binding, was given.

L123 ANSWER 31 OF 70 HCAPLUS COPYRIGHT 2002 ACS
2000:168136 Document No. 132:217151 Fluorinated butyric acids and their derivatives as inhibitors of matrix metalloproteinases, their preparation, and pharmaceutical compositions containing them. Roth, Bruce David; O'Brien, Patrick Michael; Sliskovic, Drago Robert (Warner-Lambert Company, USA). U.S. US 6037361 A 20000314, 18 pp. (English). CODEN: USXXAM. APPLICATION: US 1998-36751 19980309.

AB Fluorinated butyric acids and derivs., methods for their prepn., and pharmaceutical compns. contg. them are described which are useful as inhibitors of matrix metalloproteinases, particularly gelatinase A (72 kD gelatinase) and stromelysin-1, and also collagenase, matrilysin, and MMP-13, and for the treatment of **multiple sclerosis**, atherosclerotic plaque rupture, aortic aneurism, heart failure, restenosis, periodontal disease, corneal ulceration, burns, decubital ulcers, wound healing, cancer, **inflammation**, pain, **arthritis**, or other **autoimmune** or **inflammatory** disorders dependent on tissue invasion by leukocytes or other activated migrating cells, acute and chronic **neurodegenerative** disorders including stroke, head trauma, spinal cord injury, **Alzheimer**'s disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, **Parkinson**'s disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy. Prepn. of e.g. 4-dibenzofuran-2-yl-3,3-difluoro-4-oxobutyric acid is described.

L123 ANSWER 32 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001017499 EMBASE **Alzheimer**'s disease: Clinical treatment options. Reichman W.E.. American Journal of Managed Care 6/22 SUPPL. (S1125-S1138) 2000.
Refs: 25.
ISSN: 1088-0224. CODEN: AJMCFY. Pub. Country: United States. Language: English. Summary Language: English.

AB Comprehensive treatment of **Alzheimer**'s disease (AD) requires thorough caregiver support and a thoughtful and informed use of medications for cognition enhancement, neuroprotection, and the treatment of disturbed behavior. Current treatments such as the cholinesterase inhibitors donepezil and rivastigmine can slow the progression of cognitive and functional deficits in AD over the short term. Sustained improvement and possible disease modification that result from the use of these medications are being evaluated in long-term studies. Treatment with alpha-tocopherol (vitamin E) has been shown to delay the progression of nursing home admission in patients with mild-to-moderate AD. Although antioxidant, anti-**inflammatory**, and other treatment strategies are promising, recent studies of the treatment of AD with estrogen or prednisone have produced disappointing results. For managing the behavioral symptoms that commonly accompany AD (eg, delusions, aggression, depression, anxiety, irritability), various antipsychotics, antidepressants, and anticonvulsants have been effective in carefully selected patients.

L123 ANSWER 33 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2001012793 EMBASE Depression in alpha-synucleinopathies: Prevalence, pathophysiology and treatment. Stefanova N.; Seppi K.; Scherfler C.; Puschban Z.; Wenning G.K.. G.K. Wenning, Department of Neurology,

Searched by: Mary Hale 308-4258 CM-1 1E01

University Hospital Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria. gregor.wenning@uibk.ac.at. Journal of Neural Transmission, Supplement -/60 (335-343) 2000.
Refs: 44.
ISSN: 0303-6995. CODEN: JNTSD4. Pub. Country: Austria. Language: English. Summary Language: English.

AB **Parkinson**'s disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA) are increasingly recognized as alpha-synucleinopathies, i.e. **neurodegenerative** disorders that share a common subcellular pathology characterized by alpha-synuclein abnormal aggregation. In the present review we focus on depression in alpha-synucleinopathies, discussing epidemiological, pathophysiological and treatment aspects of this frequently disabling clinical feature which may occur in PD, DLB and MSA alike.

L123 ANSWER 34 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000440643 EMBASE Affective disorders in **Parkinson**'s disease.
Kremer J.; Starkstein S.E.. Dr. J. Kremer, FLENI, Montaneses 2325, 1428 Buenos Aires, Argentina. jkremer@fleni.org.ar. International Review of Psychiatry 12/4 (290-297) 2000.
Refs: 56.
ISSN: 0954-0261. CODEN: IRPSE2. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB This article reviews the prevalence, phenomenology, main clinical correlates, potential mechanisms, and treatment modalities of depression in **Parkinson**'s disease (PD). In cross-sectional samples of PD patients attending a **neurology** unit the prevalence of depression is about 40%, but prevalences may be lower in epidemiological samples. Both psychological and autonomic symptoms of depression are specific to the depressive syndrome of PD, except for the symptoms of anergia, motor retardation, and early morning awakening. Depression may start before the onset of motor symptoms, and most patients with PD may eventually develop depression at some point during their longitudinal evolution. Follow-up studies suggest that PD patients with major depression have a significantly faster decline in activities of daily living and cognitive functions, and a faster progression along the stages of the illness as compared to non-depressed PD patients. Finally, there are few controlled studies of antidepressants in PD, but tricyclic compounds demonstrated adequate efficacy and tolerability.

L123 ANSWER 35 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000238858 EMBASE [Diagnostic steps in possible **Alzheimer** dementia before starting with new therapeutics]. DIAGNOSTISCHE SCHRITTE BEI **ALZHEIMER**-DEMENZ VOR THERAPIEBEGINN MIT NEUEN ANTIDEMENTIVA. Kropp S.; Schlimme J.; Bleich S.; Wiltfang J.; Dietrich D.E.; Emrich H.M.. Dr. S. Kropp, Klinische Psychiatrie/Psychotherapie, Medizinische Hochschule Hannover, 30623 Hannover, Germany. kropp.stefan@mh-hannover.de. Fortschritte der Neurologie Psychiatrie 68/6 (257-261) 2000.
Refs: 32.
ISSN: 0720-4299. CODEN: FNPGA3. Pub. Country: Germany. Language: German. Summary Language: English; German.

AB The dementia of the **Alzheimer** type (DAT) is a chronic **neurodegenerative** illness. It will continue to increase because of rising life expectancy in the industrialized countries. Apart from the physicians interest to treat, there is also an economically justified interest to reduce the disease progression in this group of patients. The main intention of the treating physicians is to keep their patients independent as long as possible. Up to now **Alzheimer**'s disease can only be treated symptomatically. The verified diagnosis of DAT still depends on the neuropathological investigation of brain tissue. Therefore

the clinical diagnosis of DAT during lifetime should be supported by chemical analysis of typical changes in the cerebrospinal fluid (CSF) at an early stage. Meanwhile, several therapeutics with proven effectiveness in clinical studies are certified for the symptomatic treatment of DAT. However, these therapeutics are still relatively expansive. Due to this fact the clinical diagnosis of DAT should be supported by clinical-chemical markers before the beginning of such a treatment. In this paper we present the diagnostic steps in dementia patients, who are examined in our departments. Patients suspicious of DAT always are asked for a spinal tap in addition to other diagnostic tools. In case of a typical clinical constellation, the exclusion of a primarily vascular dementia as well as the proof of decreased A.beta.1-42 peptides and an increased tau protein in CSF we recommend the new drugs for DAT as meaningful and justified therapeutics to yield optimal treatment.

L123 ANSWER 36 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2000336061 EMBASE The CYP2C19 enzyme polymorphism. Wedlund P.J.. Dr. P.J. Wedlund, College of Pharmacy, Eastern State Hosp. Research Center, University of Kentucky, Lexington, KY 40536-0082, United States. Pharmacology 61/3 (174-183) 2000.
Refs: 106.
ISSN: 0031-7012. CODEN: PHMGBN. Pub. Country: Switzerland. Language: English. Summary Language: English.
AB The genetic test is gradually replacing probe drugs as the primary tool for screening populations for the CYP2C19 polymorphism. A full appreciation for the clinical and toxicological relevance of this genetic variation is presently limited. Further research is needed in several areas. The development and use of 3-D models of the CYP2C19 enzyme to automate and increase the rate at which CYP2C19 substrates are identified could reap great benefits. Meanwhile, clinical research should begin to determine whether the CYP2C19 polymorphism affects therapeutic outcomes and toxicity of drugs in actual patient settings. Combining research efforts in molecular modeling, genetic testing, clinical and epidemiological research will be required if better appreciation of this genetic variation and its importance in the population at large is to emerge. Copyright (C) 2000 S. Karger AG, Basel.

L123 ANSWER 37 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:390467 Document No.: PREV199900390467. SSRI-induced **Parkinsonism** may be an early sign of future **Parkinson**'s disease. Gonul, Ali Saffet (1); Aksu, Murat (1). (1) Kayseri Turkey. Journal of Clinical Psychiatry, (June, 1999) Vol. 60, No. 6, pp. 410. ISSN: 0160-6689. Language: English.

L123 ANSWER 38 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1999:764013 Document No. 132:12201 Preparation of biarylalkylhydroxamic acids and related compounds as matrix metalloprotease inhibitors.. Kluender, Harold C. E.; Brittelli, David R.; Schoen, William R.; Ha, Sookhee N. (Bayer Corporation, USA). PCT Int. Appl. WO 9961413 A1 19991202, 94 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US11481 19990525. PRIORITY: US 1998-85909 19980527.
AB TxABDEG [A = Ph, thienyl, furyl, pyrrolyl, oxazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, etc.; B = bond,

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thienylene, furylene, phenylene, furylene, imidazolylene, pyridinylene, pyrazinylene, pyridazinylene, etc.; T = halo, alkyl, haloalkyl, haloalkoxy, alkenyl, alkynyl, etc.; x = 0, 1, 2; D = CO, CH(OH), C:NN(R2)2, C:NOR2; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; E = 2-3 C atom chain bearing 1-3 substituents; G = COCH2OH, CONHOH, CONHSO2R3; R3 = alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl], were prepd. as matrix metalloproteinase inhibitors (no data). Thus, 4-(biphen-4-yl)-4-oxobutyric acid in EtOAc/CH2Cl2 was treated with CH2N2 in Et2O to give 100% Me ester, which was added to a soln. of NH2OH.HCl and KOH in MeOH/H2O to give 4-Ph6H4C(:NOH)CH2CH2CONOH.

L123 ANSWER 39 OF 70 HCAPLUS COPYRIGHT 2002 ACS

1999:595127 Document No. 131:228643 Preparation of oxalylaminothiophene derivatives as modulators of protein tyrosine phosphatases (PTPases). Richter, Lutz Stefan; Andersen, Henrik Sune; Vagner, Josef; Jeppesen, Claus Bekker; Moller, Niels Peter Hundahl; Branner, Sven; Jeppesen, Lone; Olsen, Ole Hvilsted; Iversen, Lars Fogh; Holsworth, Daniel Dale; Axe, Frank Urban; Ge, Yu; Jones, Todd Kevin; Ripka, Wiliam Charles; Uyeda, Roy Teruyuki; Su, Jing; Bakir, Farid; Judge, Luke Milburn (Novo Nordisk A/S, Den.; Ontogen Corporation; Richter, Birgith). PCT Int. Appl. WO 9946237 A1 19990916, 230 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-DK126 19990312. PRIORITY: DK 1998-350 19980312; DK 1998-345 19980312; DK 1998-343 19980312; DK 1998-342 19980312; DK 1998-344 19980312; DK 1998-347 19980312; DK 1998-346 19980312; DK 1998-348 19980312; DK 1998-479 19980403; DK 1998-472 19980403; DK 1998-473 19980403; DK 1998-478 19980403; DK 1998-475 19980403; DK 1998-474 19980403; DK 1998-476 19980403; DK 1998-480 19980403; US 1998-PV82912 19980424; DK 1998-667 19980515; US 1998-PV88115 19980605; DK 1998-939 19980715.

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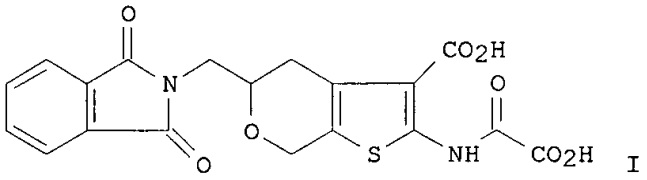

I

AB Oxalylaminoheterocycles (e.g., oxalylaminothiophene and oxalylaminothienopyran derivs., etc.) were prepd. as inhibitors of Protein Tyrosine Phosphatases (PTPases), such as PTP1B, TC-PTP, CD45, SHP-1, SHP-2, PTP.alpha., PTP.epsilon., PTP.mu., PTP.delta., PTP.sigma., PTP.zeta., PTP.beta., PTPD1, PTPD2, PTPH1, PTP-MEG1, PTP-LAR, and HePTP. These compds. are indicated in the management or treatment of a broad range of diseases such as **autoimmune** diseases, acute and chronic **inflammation**, osteoporosis, various forms of cancer and malignant diseases, and type I diabetes and type II diabetes. For instance, 2-amino-5-hydroxymethyl-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid tert-Bu ester (prepn. given) was reacted with phthalimide in THF,

PPh3, and DIAD to form the 5-phthalimidomethyl deriv. (47%). The amine was amidated with imidazol-1-yloxoacetic acid tert-Bu ester in CH2Cl2 and TEA (99%), followed by hydrolysis of the ester function with TFA in CH2Cl2, to give 5-(1,3-dioxo-1,3-dihydroisoindol-2-ylmethyl)-2-(oxalylamino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid (I) in 57% yield. In an in vitro test against PTP1B expressed in E. coli and purified by known methods, Ki values at various inhibitor concns. were detd. An anal. of selectivity of two PTPase inhibitors against PTP1B, PTP-LAR, PTP.epsilon., CD45, and PTP.beta. showed that one compd. of the invention is a non-selective inhibitor, whereas another behaves like a selective inhibitor.

L123 ANSWER 40 OF 70 HCAPLUS COPYRIGHT 2002 ACS

1999:595124 Document No. 131:228549 Preparation of (oxalylamino)benzoic acid derivatives and analogs as modulators of protein tyrosine phosphatases (PTPases). Richter, Lutz Stefan; Andersen, Henrik Sune; Vagner, Josef; Jeppesen, Claus Bekker; Moller, Niels Peter Hundahl; Branner, Sven; Su, Jing; Bakir, Farid; Judge, Luke Milburn (Novo Nordisk A/S, Den.; Ontogen Corporation). PCT Int. Appl. WO 9946236 A1 19990916, 100 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-DK122 19990311. PRIORITY: DK 1998-342 19980312; DK 1998-345 19980312; DK 1998-472 19980403; DK 1998-479 19980403; DK 1998-940 19980715.

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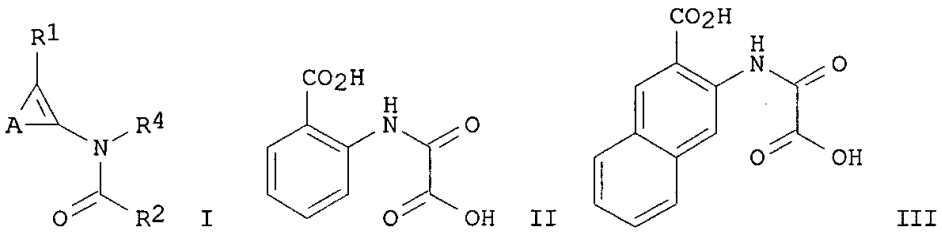

AB Title compds. I [A = atoms to complete (un)substituted Ph, biphenyl, indenyl, fluorenyl, naphthyl, pyridyl, pyridazinyl, pyrimidinyl, or pyrazinyl nucleus; R1 = H, acyl, CO2H, OH or derivs., CF3, NO2, cyano, SO3H, amino, various 5-membered heterocycles, etc.; R2 = acyl, CO2H, OH or derivs., CF3, NO2, cyano, SO3H, (un)substituted NH2 or PO3H2, various 5-membered heterocycles, etc.; R4 = H, OH, alkyl, (un)substituted aryl or aralkyl, (un)substituted NH2, alkoxy] were prepd. as inhibitors of protein tyrosine phosphatases (PTPases), such as PTP1B, CD45, SHP-1, SHP-2, PTP.alpha., LAR, and HePTP. The compds. are useful in the treatment of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance, obesity, **immune** dysfunctions including **autoimmunity** diseases with dysfunctions of the coagulation system, allergic diseases including asthma, osteoporosis, proliferative disorders including cancer and psoriasis, diseases with decreased or increased synthesis or effects of growth hormone, diseases with decreased or increased synthesis of hormones or cytokines that regulate the release of/or response to growth hormone, diseases of the brain including

Alzheimer's disease and schizophrenia, and infectious diseases. For instance, anthranilic acid was amidated with Et oxalyl chloride in THF (94%), followed by hydrolysis of the ester function with NaOH in aq. EtOH soln. (81%), to give the title compd. II. In an in vitro test against PTP1B expressed in E. coli and purified by known methods, II had a Ki of 20 .mu.M, and the similarly prepd. 2,3-substituted naphthalene analog III had a Ki of 9.9 .mu.M.

L123 ANSWER 41 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1999:297406 Document No. 130:325093 Preparation of substituted isoquinolines as anticonvulsants. Thompson, Mervyn; Harling, John David; Edwards, Peter David (Smithkline Beecham Plc, UK). PCT Int. Appl. WO 9921836 A1 19990506, 72 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB3165 19981022. PRIORITY: GB 1997-22537 19971024; GB 1997-26663 19971217.

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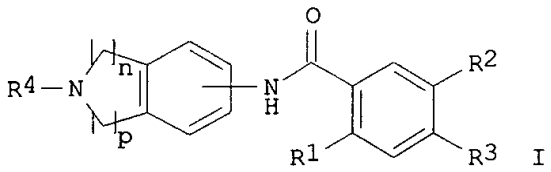

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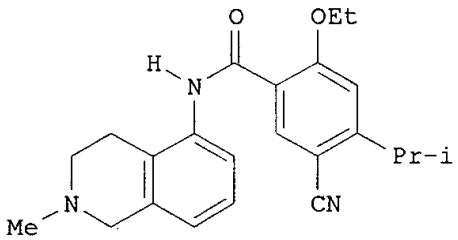

II

AB The title compds. [I; n, p = 1-4 and n + p = 2-5; R1 = H, cycloalkylO, etc.; R2 = H, halo, CN, etc.; R3 = H, halo, NO2, etc.; R2R3 = (un)substituted (un)satd. carbocyclic ring; R4 = H, alkyl, alkenyl, etc.], useful as anticonvulsants, were prepd. Thus, conversion of 2-ethoxy-4-isopropyl-5-cyanobenzoic acid into the acid chloride followed by coupling with 5-amino-2-methyl-1,2,3,4-tetrahydroisoquinoline afforded 60% II.HCl which showed a 336% increase in seizure threshold for rat MEST. Compds. I are useful in the prophylaxis and treatment of anxiety, mania, depression, panic disorders and/or aggression, disorders assocd. with a subarachnoid hemorrhage or neural shock, the effects assocd. with withdrawal from substances of abuse such as cocaine, nicotine, alc. and benzodiazepines, disorders treatable and/or preventable with anti-convulsive agents, such as epilepsy including post-traumatic epilepsy, **Parkinson**'s disease, psychosis, migraine, cerebral ischemia, **Alzheimer**'s disease and other degenerative diseases such as Huntington's chorea, schizophrenia, obsessive compulsive disorders (OCD), **neurol**. deficits assocd. with AIDS, sleep disorders (including circadian rhythm disorders, insomnia and narcolepsy), tics (e.g. Giles de la Tourette's syndrome), traumatic brain injury, tinnitus,

neuralgia, esp. trigeminal neuralgia, neuropathic pain, dental pain, cancer pain, inappropriate neuronal activity resulting in neurodysthesias in diseases such as diabetes, **multiple sclerosis** (**MS**) and motor neuron disease, ataxias, muscular rigidity (spasticity), temporomandibular joint dysfunction and amyotrophic lateral sclerosis (ALS).

L123 ANSWER 42 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1999:48694 Document No. 130:124898 Preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivatives as MEK inhibitors. Barrett, Stephen Douglas; Bridges, Alexander James; Cody, Donna Reynolds; Doherty, Annette Marian; Dudley, David Thomas; Saltiel, Alan Robert; Schroeder, Mel Conrad; Tecle, Haile (Warner-Lambert Company, USA). PCT Int. Appl. WO 9901421 A1 19990114, 67 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US13105 19980624. PRIORITY: US 1997-51433 19970701.

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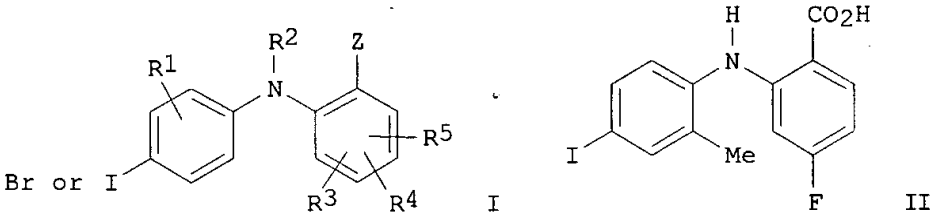


AB The title compds. [I; R1 = H, OH, C1-8 alkyl, etc.; R2 = H; R3-R5 = H, OH, halo, etc.; Z = COOR7, tetrazolyl, CONR6R7, etc.; R6, R7 = H, C1-8 alkyl, C2-8 alkenyl, etc.], which are potent inhibitors of MEK and, as such, are effective in treating cancer and other proliferative diseases such as **inflammation**, psoriasis and restenosis, as well as stroke, heart failure, and **immunodeficiency** disorders, were prepd. and formulated. Thus, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethylbenzene soln. followed by addn. of 2,4-difluorobenzoic acid in THF afforded II which showed IC50 of 0.019 .mu.M against MEK in vitro.

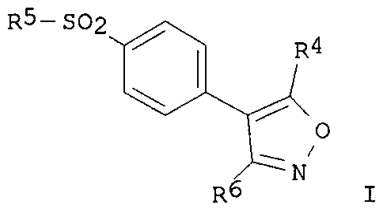
L123 ANSWER 43 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1999:205305 Document No. 130:232515 Methods useful for the treatment of **neurological** and mental disorders related to deficient serotonin neurotransmission and impaired pineal melatonin functions. Sandyk, Reuven (USA). U.S. US 5885976 A 19990323, 35 pp., Cont.-in-part of U.S. 5,691,324. (English). CODEN: USXXAM. APPLICATION: US 1997-978383 19971125. PRIORITY: US 1995-437273 19950508.

AB A compn. is described which is useful for treating **neurol**. and mental disorders which are assocd. with and/or related pathogenetically to deficient serotonin neurotransmission and impaired pineal melatonin functions in humans the compn. being administered in combination with a sufficient amt. of an AC pulsed magnetic field alone or in conjunction with a DC magnetic field and a sufficient amt. of random noise to the brain of a human in need of such treatment which compn. comprises an effective amt. of a compn. which increases serotonin transmission to the

human to be treated. A method of treating **neurol**. and mental disorders which are assocd. with and/or related pathogenetically to deficient serotonin neurotransmission and impaired pineal melatonin functions in humans is described which comprises administering to a human in need thereof an effective amt. of a compn. which increases serotonin transmission to the human to be treated followed by the application to the brain of the human of a sufficient amt. of AC pulsed magnetic field alone, or in combination with a DC magnetic field and low frequency random noise, of proper intensity, frequency, waveform, wave symmetry and phase shift of the wave to treat the disorder.

L123 ANSWER 44 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1999:45215 Document No. 130:110269 Preparation of isoxazole compounds as cyclooxygenase inhibitors. Talley, John J. (G. D. Searle & Co., USA). U.S. US 5859257 A 19990112, 52 pp., Cont.-in-part of U.S. 5,633,272. (English). CODEN: USXXAM. APPLICATION: US 1996-702417 19960814. PRIORITY: US 1995-387680 19950213; US 1995-473884 19950607.

GI



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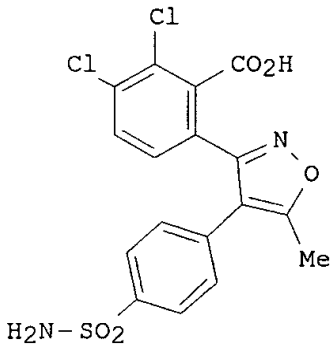


II

AB Claimed is a method of prepg. title compds. I [R4 = alkyl, etc.; R5 = amino; R6 = (un)substituted phenyl] by treatment of a diphenylethanone deriv. with hydroxylamine, treating said oxime with base and an acylating agent to form a diphenylisoxazoline deriv., and forming the (isoxazol-4-yl)benzenesulfonamide by treatment of the isoxazoline with chlorosulfonic acid and ammonia. The title compd. II in vitro showed IC50 values of 0.4 .mu.M and > 100 .mu.M against COX-2 and COX-1, resp.

L123 ANSWER 45 OF 70 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
1999:218705 Document No. 130:291493 Adverse reactions of selective serotonin reuptake inhibitors: reports from a spontaneous reporting system. Spigset, Olav (Adverse Drug Reactions Monitoring Center, Division of Clinical Pharmacology, Norrland University Hospital, Umea, Swed.). Drug Safety, 20(3), 277-287 (English) 1999. CODEN: DRSAEA. ISSN: 0114-5916. Publisher: Adis International Ltd..

AB The selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors (SSRIs) are extensively used in the treatment of depression, panic disorder and obsessive-compulsive disorder, and are now being evaluated in the treatment of a no. of other psychiatric disorders. The aim of this study was to investigate the pattern of adverse reactions reported on SSRIs in Sweden and assess possible risk factors assocd. with the occurrence of adverse reactions to these agents. A survey was made of 1202 reports describing 1861 adverse reactions to SSRIs submitted to the Swedish Adverse Drug Reactions Advisory Committee. The most often reported adverse reactions were **neurol**. symptoms (22.4%),

Searched by: Mary Hale 308-4258 CM-1 1E01

psychiatric symptoms (19.5%) and gastrointestinal symptoms (18.0%); however, dermatol. symptoms (11.4%) and general symptoms (9.8%) were also frequent. Compared with other drugs, gastrointestinal symptoms were more often reported for fluvoxamine, psychiatric symptoms were more often reported for sertraline and dermatol. symptoms were more often reported for fluoxetine. In total, the diagnoses most frequently reported were nausea (n = 139), rash (n = 90), anxiety (n = 84), paraesthesias (n = 69), headache (n = 63) and diarrhea (n = 63). **Parkinsonism**, confusion, hallucinations, euphoria, hyponatreamia, bradycardia and hypotension were more often reported in the elderly, whereas urticaria, akathisia, and haematol., endocrinol., sexual and some visual reactions were more often reported in individuals who were younger than av. Dermatol. reactions, fatigue, hyponatremia and cough were more common in women, whereas dyskinesias/akathisia and aggression more often were seen in men. The median SSRI dosages were above av. in patients experiencing seizures, hypomania/mania, personality changes, malaise, bodyweight gain, gynaecomastia and hyperprolactinemia/galactorrhoea. Severe symptoms, such as seizures, hyponatremia and the serotonin syndrome, were rarely reported. Although the design of the study makes it difficult to draw conclusions about causality, a variety of adverse reactions were reported. Therefore, the awareness that a particular symptom in a patient treated with an SSRI might be an adverse reaction should be high.

L123 ANSWER 46 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
1999375617 EMBASE [Atypical antipsychotic drugs]. LES ANTIPSYCHOTIQUES ATYPIQUES. Massoubre C.; Lang F.. C. Massoubre, Service de Psychiatrie 52B, Hopital Bellevue, CHU de Saint-Etienne, 42055 Saint-Etienne Cedex 2, France. catherine.massoubre@wanadoo.fr. Journal de Pharmacie de Belgique 54/3 (65-71) 1999.
Refs: 11.
ISSN: 0047-2166. CODEN: JPBEAJ. Pub. Country: France. Language: French. Summary Language: English; French.
AB This paper synthetizes important information concerning principal atypical antipsychotic drugs actually used in clinical practice: classification, pharmacokinetics, therapeutic uses, side effects, contra- indications and drug interactions. These molecules have heterogeneous structures, but are more and more used because of good **neurological** tolerance, greater efficacy against negative symptoms, and for clozapin greater efficacy against resistant schizophrenia.

L123 ANSWER 47 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
1999110000 EMBASE Depression in the medical setting: Biopsychological interactions and treatment considerations. Evans D.L.; Staab J.P.; Petitto J.M.; Morrison M.F.; Szuba M.P.; Ward H.E.; Wingate B.; Luber P.; O'Reardon J.P.; Evans; Schatzberg; Nemeroff; Feighner. Dr. D.L. Evans, Department of Psychiatry, Univ. of Pennsylvania Sch. of Med., 300 Blockley Hall, 423 Guardian Dr., Philadelphia, PA 19104, United States. Journal of Clinical Psychiatry 60/SUPPL. 4 (40-56) 1999.
Refs: 194.
ISSN: 0160-6689. CODEN: JCLPDE. Pub. Country: United States. Language: English. Summary Language: English.
AB This article examines depression in 6 medical conditions: coronary artery disease (CAD), cancer, human **immunodeficiency** virus (HIV) infection, **Parkinson**'s disease, pain, and the sex hormone changes of aging. Research is beginning to define specific biological and psychological mechanisms underlying the adverse interactions between depression and these medical conditions. Antidepressant medications, psychosocial therapies, and hormonal manipulations are effective in reducing depressive symptoms. Specific psychosocial interventions may increase longevity in CAD and cancer and may enhance quality of life in

HIV infection. Newer antidepressants appear to be safer and better tolerated than older agents for medically ill patients, but do not appear to be as effective for neuropathic pain. Dopamine agonists may benefit depression associated with **Parkinson**'s disease. Hormone replacement therapy may improve subsyndromal depressive symptoms in postmenopausal women and may enhance antidepressant response for older women with major depression.

L123 ANSWER 48 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1998:527311 Document No. 129:148827 Preparation of (hetero)arylsulfonylurea derivatives as inhibitors of interleukin-1 processing and release.. Dombroski, Mark Anthony; Eggler, James Frederick (Pfizer Inc., USA). PCT Int. Appl. WO 9832733 A1 19980730, 81 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-IB1603 19971229. PRIORITY: US 1997-36979 19970129.

AB R1SO2NHCONHR2 [R1 = (substituted) alkyl, or R1, R2 = specified (substituted) 5-8 membered (heterocyclic) ring, (CH2)sXtCOY, (CH2)uC(R19):NOR20, etc.; s = 0-6; t = 0, 1; u = 0-2; X = O, imino; Y = H, OH, (substituted) alkyl, etc.; R19 = H, alkyl, perfluoroalkyl; R20 = H, alkyl, carboxyalkyl, aralkyl], were prepd. for treatment of meningitis, salpingitis, septic shock, disseminated intravascular coagulation, adult respiratory distress syndrome, **inflammation, arthritis**, cholangitis, colitis, encephalitis, endocarditis, glomerulonephritis, hepatitis, myocarditis, pancreatitis, pericarditis, reperfusion injury, vasculitis, acute and delayed hypersensitivity, graft rejection, graft-vs.-host disease, **autoimmune** diseases including Type 1 diabetes mellitus and **multiple sclerosis**, periodontal diseases, interstitial pulmonary fibrosis, cirrhosis, systemic sclerosis, keloid formation, tumors which produce IL-1 as an autocrine growth factor, cachexia, **Alzheimer**'s disease, percussion injury, depression, atherosclerosis, and osteoporosis (no data). Thus, 2-(3-aminosulfonylphenyl)propan-2-ol (prepn. given) was stirred with NaH in THF; 4-chloro-2,6-diisopropylphenyl isocyanate was added and the mixt. was refluxed 12 h to give 1-(4-chloro-2,6-diisopropylphenyl)-3-[3-(1-hydroxy-1-methylethyl)benzenesulfonyl]urea.

L123 ANSWER 49 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1998:424263 Document No. 129:95714 Preparation of new heterocyclic amides as nitric oxide production inhibitors. Yatabe, Takumi; Inoue, Takayuki; Hamashima, Hitoshi; Shima, Ichiro; Ohne, Kazuhiko; Yoshihara, Kousei; Oku, Teruo (Fujisawa Pharmaceutical Co., Ltd., Japan; Yatabe, Yoshiko; Itoh, Yoshikuni; Inoue, Takayuki; Hamashima, Hitoshi; Shima, Ichiro; Ohne, Kazuhiko; Yoshihara, Kousei; Oku, Teruo). PCT Int. Appl. WO 9827108 A2 19980625, 533 pp. DESIGNATED STATES: W: AU, CA, CN, HU, IL, JP, KR, MX, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-JP4243 19971120. PRIORITY: AU 1996-4219 19961216; AU 1997-5929 19970401; AU 1997-9030 19970909.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Searched by: Mary Hale 308-4258 CM-1 1E01

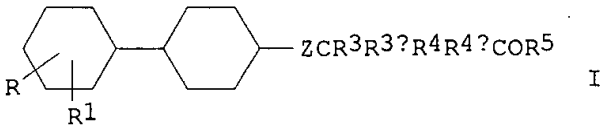
AB Title compds. I [X = S, NR9; Y = CHR3, (un)substituted phenylene; R1 = (un)substituted indolyl, (un)substituted benzofuranyl; R2 = H, phenyl-lower alkyl; R3 = H, (CH2)nR6; R4 = H, (un)substituted Ph, (un)substituted pyridyl; R5 = H, imidazolyl, Ph, nitrophenyl, phenyl-lower alkyl, optionally esterified carboxy, CONR7R8; R4R5 = CH:CHCH:CH; R6 = optionally protected OH, acyl, carboxy, acylamino, lower alkoxy, phenyl-lower alkoxy, lower alkylthio, (un)substituted Ph; R7, R8 = independently H, Ph, phenyl-lower alkyl, lower alkyl, lower alkoxy; R9 = H, lower alkyl, lower cycloalkyl, (un)substituted benzyl; m = 0, 1; n = 0-3] and pharmaceutically acceptable salts thereof are described as strong inhibitors of the prodn. of nitric oxide. Compds. I are useful for prevention and treatment of nitric oxide-mediated diseases such as adult respiratory distress syndrome, cardiovascular ischemia, myocarditis, heart failure, synovitis, shock, diabetes, diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, glomerulonephritis, peptic ulcer, **inflammatory** bowel disease, cerebral infarction, cerebral ischemia, cerebral hemorrhage, migraine, rheumatoid **arthritis**, gout, neuritis, post-herpetic neuralgia, osteoarthritis, osteoporosis, systemic **lupus** erythematosus, rejection by organ transplantation, asthma, metastasis, **Alzheimer**'s disease, **arthritis**, CNS disorders, dermatitis, hepatitis, liver cirrhosis, **multiple sclerosis**, pancreatitis, atherosclerosis, and the like in humans and animals. Thus, 2-step cyclocondensation of amino ketone II (prepn. given) with protected 3-(2-pyridyl)-L-alanine and methylamine gave protected imidazole III (Boc = Me3CO2C). Deprotection of III followed by acylation with indole-2-carboxylic acid gave desired compd. IV. IV inhibited nitric oxide prodn. 100% in murine macrophage cell line RAW264.7 at 10-5 M.

L123 ANSWER 50 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1998:424117 Document No. 129:113523 Use of matrix metalloproteinase inhibitors for treating **neurological** disorders and promoting wound healing. Bocan, Thomas Michael Andrew; Boxer, Peter Alan; Peterson, Joseph Thomas, Jr.; Schrier, Denis; White, Andrew David (Warner-Lambert Co., USA; Bocan, Thomas Michael Andrew; Boxer, Peter Alan; Peterson, Joseph Thomas, Jr.; Schrier, Denis; White, Andrew David). PCT Int. Appl. WO 9826773 A1 19980625, 163 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US21532 19971121. PRIORITY: US 1996-32753 19961217.
AB Matrix metalloproteinase inhibitors 4-RC6H4SO2NHCHR1COR2 [R = (un)substituted Ph; R1 = alkyl, phenylalkyl, phenyl; R2 = OH, alkoxy, NHOH] and 4-RC6H4C(:NR3)CR4R5CR6R7COR8 [R3 = (un)substituted OH, NH2; R4-R7 = H, F, (un)substituted alkyl; R8 = OH, SH] are useful for preventing and treating **neurol**. disorders, esp. **Alzheimer**'s, huntington's, and **Parkinson**'s diease and amyotropic lateral sclerosis, and in promoting wound healing. IC50 for matrix metalloproteinase inhibition are reported for a no. of compds. Formulations contg. (R)-4-(4-NCC6H4)C6H4SO2NHCH(CO2H)CH2Ph, (S)-4-(4-H2NC6H4)C6H4SO2NHCH(CO2H)CH2C6H4OEt-3, and 4-(4-BrC6H4)C6H4SO2NHCH(CO2H)CHMe2 are reported.

L123 ANSWER 51 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1998:175902 Document No. 128:217187 Preparation of biphenylbutyric acids and their derivatives as inhibitors of matrix metalloproteinases. Purchase, Claude Forsey, Jr.; Roth, Bruce David; White, Andrew David; Schielke,

Gerald Paul; Walker, Lary Craswell (Warner-Lambert Company, USA; Purchase, Claude Forsey, Jr.; Roth, Bruce David; White, Andrew David; Schielke, Gerald Paul; Walker, Lary Craswell). PCT Int. Appl. WO 9809940 A1 19980312, 121 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US14852 19970822. PRIORITY: US 1996-25814 19960904; US 1996-27138 19961002; US 1997-54905 19970806.

GI



I

AB Biphenylbutyric acid derivs. I [R, R1 = H, alkyl, halo, cyano, OCF3, etc.; Z = CO, CS, CH(OH), CF2, CHF; R3, R3a, R4, R4a = H, F, alkyl, (CH2)naryl with n = 1-6, etc; R5 = OH, SH, alkoxy, cycloalkoxy, etc.], inhibitors of matrix metalloproteinases, particularly gelatinase A (72 kD gelatinase) and stromelysin-1 and for the treatment of **multiple sclerosis**, atherosclerotic plaque rupture, aortic aneurism, heart failure, restenosis, periodontal disease, corneal ulceration, treatment of burns, decubital ulcers, wound healing, cancer, **inflammation**, pain, **arthritis**, or other **autoimmune** or **inflammatory** disorders dependent upon tissue invasion by leukocytes or other activated migrating cells, acute and chronic **neurodegenerative** disorders including stroke, head trauma, spinal cord injury, **Alzheimer**'s disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, **Parkinson**'s disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy, were prepd. E.g., reaction of 4-chlorobiphenyl and succinic anhydride in presence of AlCl3 gave 4-(4'-chlorobiphenyl-4-yl)-4-oxobutyric acid. Treatment of this product with hydroxylamine hydrochloride gave 4-(4'-chlorobiphenyl-4-yl)-4-(hydroxyimino)butyric acid. I are inhibitors of gelatinase A and stromelysin-1.

L123 ANSWER 52 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

1998205948 EMBASE Selective serotonin-reuptake inhibitor-induced movement disorders. Gerber P.E.; Lynd L.D.; Leo R.J.. Dr. P.E. Gerber, Department of Pharmacy, British Columbia's Children's Hosp., 4480 Oak St., Vancouver, BC V6H 3V4, Canada. Annals of Pharmacotherapy 32/6 (692-698+712-714) 1998.
Refs: 20.
ISSN: 1060-0280. CODEN: APHRER. Pub. Country: United States. Language: English. Summary Language: English; Spanish; French.

AB OBJECTIVE: To compile and evaluate all available data suggesting an association between selective serotonin-reuptake inhibitor (SSRI) administration and the occurrence of movement disorders, and to characterize these reactions in terms of onset, duration, treatment and outcome, and potential predisposing factors. METHODOLOGY: Reports of movement disorders were identified by conducting a comprehensive literature search that included tertiary adverse drug reaction resources, MEDLINE, EmBASE, Biological Abstracts, Current Contents, Reactions,

Searched by: Mary Hale 308-4258 CM-1 1E01

ClinAlert, and International Pharmaceutical Abstracts. In addition, reports were solicited from the Canadian proprietary manufacturers of SSRIs, and from the Therapeutic Products Program of Health Canada. Each case was then classified according to the description of the movement disorder, based on predefined diagnostic criteria. RESULTS: A total of 127 published reports of SSRI-induced movement disorders were identified involving akathisia (n = 30), dystonia (19), dyskinesia (12), tardive dyskinesia (6), **parkinsonism** (25), and 15 cases of mixed disorders. Ten isolated cases of bruxism were identified. Ten additional reports could not be classified. Manufacturers of SSRIs provided 49 reports of akathisia, 44 of dystonia, 208 of dyskinesia, 76 of tardive dyskinesia, 516 of **parkinsonism**, and 60 of bruxism. Treatment strategies included discontinuation of the SSRI; dosage reduction; or the addition of a benzodiazepine, .beta.-blocker, or anticholinergic agent. CONCLUSIONS: SSRI use appears to be associated with the development of movement disorders, as either a direct result of the drug or exacerbation of an underlying condition. Predisposing factors may include the use of neuroleptics, existing **neurologic** diagnoses, or preexisting movement disorders. Clinicians should be cognizant of the potential for these reactions, as prompt recognition and management is essential in preventing potentially significant patient morbidity.

L123 ANSWER 53 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

1998168838 EMBASE Idebenone: A review of its use in mild to moderate **Alzheimer**'s disease. Adkins J.C.; Noble S.. J.C. Adkins, Adis International Limited, 41 Centorian Drive, Mairangi Bay, Auckland 10, New Zealand. demail@adis.co.nz. CNS Drugs 9/5 (403-419) 1998.
Refs: 70.
ISSN: 1172-7047. CODEN: CNDREF. Pub. Country: New Zealand. Language: English. Summary Language: English.

AB Idebenone is a benzoquinone derivative which is structurally related to ubiquinone, a component of the respiratory chain. Although the precise mechanism of action of the drug is unknown, preclinical studies suggest that idebenone may exert cytoprotective properties by acting as a free radical scavenger. In addition, it also appears to improve cerebral metabolism, correct neurotransmitter defects and enhance memory and learning. Oral idebenone appears to improve cognitive function and behavioural deficits in patients with mild to moderate **Alzheimer**'s disease. In 2 large double-blind placebo-controlled trials, idebenone 270 or 360 mg/day for up to 12 months produced a mean improvement of 1.6 to 3.9 points in the total score of the **Alzheimer**'s Disease Assessment Scale (ADAS-Total) relative to placebo. After 12 months of treatment, improvements in ADAS-Total versus baseline were 10.3% with placebo, 14.7% with idebenone 270 mg/day and 19.6% with idebenone 360 mg/day, 34.1% of patients treated with idebenone 360 mg/day were judged to have improved when assessed according to measures of cognition, behaviour and clinician-related global outcome measures. Notably, patients with a lesser degree of cognitive impairment (ADAS-Total <20) appear less likely to benefit from idebenone therapy. Idebenone was well tolerated when administered for up to 12 months to patients with **Alzheimer**'s disease, and no significant changes in vital signs or laboratory values were reported. Thus, although comparisons with other agents are currently lacking, available data suggest that idebenone will be a useful therapeutic option for the management of **Alzheimer**'s disease. Because of their different mechanisms of action, combination therapy with idebenone and a cholinesterase inhibitor mar also be a possibility in the future. However, studies are necessary to assess the feasibility of such an approach for the treatment of **Alzheimer**'s disease.

L123 ANSWER 54 OF 70 HCAPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 1E01

1998:42280 Document No. 128:97720 Use of nipecotic acid or guvacine derivatives for the manufacture of a medicament for the treatment of post-ischemic **neurodegenerative** disorders. Regan, Ciaran (University College Dublin, Ire.; Regan, Ciaran). PCT Int. Appl. WO 9749403 A1 19971231, 26 pp. DESIGNATED STATES: W: AU, CA, JP, MX; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-IB791 19970626. PRIORITY: US 1996-673218 19960627.

AB A method is disclosed for treating a **neurodegenerative** dementia, e.g. **Alzheimer**'s disease, by administering a neuroprotective amt. of a lipophilic deriv. of nipecotic acid (piperidine-3-carboxylic acid) or guvacine (1,2,5,6-tetrahydropyridine-3-carboxylic acid).

L123 ANSWER 55 OF 70 HCAPLUS COPYRIGHT 2002 ACS

1997:436213 Document No. 127:55919 Hydroxylamine derivatives useful for enhancing molecular chaperon production and the preparation thereof. Vigh, Laszlo; Literati Nagy, Peter; Szilbereky, Jeno; Uerogdi, Laszlo; Jednakovits, Andrea; Jaszlits, Laszlo; Biro, Katalin; Marvanyos, Ede; Barabas, Mihaly; Hegedues, Erzsebet; Koranyi, Laszlo; Kuerthy, Maria; Balogh, Gabor; Horvath, Ibolya; Torok, Zsolt; Udvardy, Eva; Dorman, Gyorgy; Medzihradszky, Denes; Mezes, Bea; Kovacs, Eszter; Duda, Erno; Farkas, Beatrix; Glatz, Attila; et al. (Hung.). PCT Int. Appl. WO 9716439 A1 19970509, 179 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CN, CZ, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-HU64 19961101. PRIORITY: HU 1995-9503141 19951102.

AB A method of increasing expression of a mol. chaperon by a cell and/or enhancing the activity of a mol. chaperon in cells is provided. The method comprises treating a cell that is exposed to a physiol. stress which induces expression of a mol. chaperon by the cell with an effective amt. of a certain hydroxylamine deriv. to increase the stress. Alternatively, a hydroxylamine deriv. can be administrated to a cell before it is exposed to a physiol. stress which induces expression of a mol. chaperon by the cell. Preferably, the cell to which a hydroxylamine deriv. is administered is a eukaryotic cell. The invention also provides novel hydroxylamine derivs. falling within the scope of the formulas AZC(X):NOR (A = alkyl, substituted alkyl, aralkyl, substituted aralkyl, heteroaryl, etc.; Z = covalent bond, O, or NR3, where R3 = H, alkyl, substituted alkyl, aryl, etc.; R = alkyl or substituted alkyl; X = halo, substituted hydroxy or amino, substituted amino; R' = H, alkyl, substituted alkyl, aryl, substituted aryl, etc.) and AZC(:X)N(R')OR (A = alkyl, substituted alkyl, aralkyl, substituted aralkyl, heteroaryl, etc.; Z = covalent bond, O, or NR3, where R3 = H, alkyl, substituted alkyl, aryl, etc.; R = alkyl or substituted alkyl; X =O, imino, or substituted imino; R' = H, alkyl, substituted alkyl, aryl, substituted aryl, etc.) as well as pharmaceutical and/or cosmetic compns. comprising the said compds.

L123 ANSWER 56 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

97319055 EMBASE Document No.: 1997319055. [Neuropsychiatric syndromes]. LES TROUBLES DU COMPORTEMENT D'ORIGINE **NEUROLOGIQUE**. Vuadens P.; Regli F.. Dr. P. Vuadens, Service de Neurologie, CHUV, 1011 Lausanne, Switzerland. Revue Medicale de la Suisse Romande 117/9 (671-677) 1997. ISSN: 0035-3655. CODEN: RMSRA6. Pub. Country: Switzerland. Language: French. Summary Language: English; French.

AB The modifications of behavior related to **neurological** diseases are various and important to be correctly diagnosed. The purpose of this article is to present the clinical features of main neuropsychiatric syndromes: depression, delusions, anxiety, obsessive-compulsive syndrome. The differential diagnosis is also developed. The appropriate treatment is

discussed.

L123 ANSWER 57 OF 70 MEDLINE DUPLICATE 3
97305387 Document Number: 97305387. PubMed ID: 9161652. Fluvoxamine for stereotypic behavior in patients with dementia. Trappler B; Vinuela L M. (Department of Psychiatry, State University of New York, Health Science Center at Brooklyn 11203, USA.) ANNALS OF PHARMACOTHERAPY, (1997 May) 31 (5) 578-81. Journal code: 9203131. ISSN: 1060-0280. Pub. country: United States. Language: English.

AB OBJECTIVE: To describe the effects of treatment with the selective serotonin reuptake inhibitor fluvoxamine on three patients with advanced dementia who developed a stereotypic movement disorder. CASE SUMMARY: Three patients in a skilled nursing facility were referred by their primary physicians for psychiatric consultation to assist with the management of stereotypic behaviors. The patients received a standard medical, **neurologic**, and psychiatric workup for dementia. Two of the patients were diagnosed with dementia of the **Alzheimer** type and the other patient was diagnosed with vascular dementia. All three patients were started on fluvoxamine 25 mg/d; behaviors were monitored daily by the nursing staff and their primary care physicians and weekly by their psychiatrist using the Abnormal Involuntary Movement Scales. The dosage was titrated upward weekly to a maximum dosage of 150 mg/d. RESULTS: Two patients showed complete resolution of their stereotypic behaviors by week 6. The third patient showed noticeable improvement with some residual movements after 8 weeks of treatment. CONCLUSIONS: Fluvoxamine appeared effective in the control of stereotypic behaviors in three patients with advanced dementia.

L123 ANSWER 58 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
97297799 EMBASE Document No.: 1997297799. Incidence of antidepressant drug use in older adults and association with chronic diseases: The Rotterdam Study. Egberts A.C.G.; Leufkens H.G.M.; Hofman A.; Hoes A.W.. A.W. Hoes, Dept. Epidemiology/Biostatistics, Erasmus University, Medical School, P.O. Box 1738, 3000 DR Rotterdam, Netherlands. International Clinical Psychopharmacology 12/4 (217-223) 1997.
Refs: 32.
ISSN: 0268-1315. CODEN: ICLPE4. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB A follow-up study was conducted among men and women aged 55 years and over living in the community in order to estimate the incidence of initiation of antidepressant drug use and the association with chronic diseases. The study population consisted of 7,812 individuals. Overall, the incidence density for starting therapy with an antidepressant drug was 13.5 per 1000 person-years. The cumulative incidences after 1, 2 and 3 years were 1.3, 2.7 and 4.0%, respectively. The incidence in women was almost twice that in men and slightly higher in participants older than 70 years than in those younger than 70 years. The majority of the antidepressants prescribed were tricyclic antidepressants (65%), followed by selective serotonin reuptake inhibitors (23%) and other (12%) antidepressants. Only a minority (23%) received a dose considered effective for the indication of depression. Selective serotonin reuptake inhibitors were more often prescribed in an adequate dosage (68%) than were tricyclic antidepressants (12%) and other antidepressants (8%). Of the chronic diseases studied, only osteoarthritis and a history of stroke were predictors of initiation of antidepressant drug use after adjustment for age, sex and medical consumption. Hypertension, history of myocardial infarction, diabetes mellitus, rheumatoid **arthritis**, glaucoma, cognitive impairment and **Parkinson**'s disease were not associated with future antidepressant drug use. No relevant differences were observed with respect to the choice of type of antidepressant drug among patients with

chronic diseases. The present study indicates that each year antidepressant drug therapy is initiated in approximately 1.3% of the elderly. In general, the presence of chronic somatic diseases was not predictive of initiation of antidepressant drugs. Tricyclic antidepressants in this age group and in patients with certain chronic diseases may not be the optimal choice given their side-effects profile and drug-drug and drug-disease interactions. The predominance of these agents in the present study calls for further attention.

L123 ANSWER 59 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1997:303746 Document No.: PREV199799602949. Extrapyramidal side-effects in elderly patients exposed to selective serotonin reuptake inhibitors. Gormley, Niall; Watters, Liam; Lawlor, Brian A. (1). (1) Dep. Psychiatry Elderly, St. James's Hosp., Dublin 8 Ireland. Human Psychopharmacology, (1997) Vol. 12, No. 2, pp. 139-143. ISSN: 0885-6222. Language: English.
AB Extrapyramidal side-effects (EPSE) are reported to occur in less than one per 1000 patients treated with selective serotonin reuptake inhibitors (SSRIs). However, it might be expected that EPSE might occur more frequently in elderly patients. We assessed the case notes of all elderly patients admitted to an acute psychiatric unit over a 3-year period and the charts of an equivalent number of elderly patients seen by a geriatric psychiatry consultation/liaison team on the general hospital's medical wards to determine the prevalence of EPSE following exposure to SSRIs. Records from 136 admissions and 140 consultations were assessed. A total of 67 patients were prescribed an SSRI. Four patients (6 per cent) developed an extrapyramidal reaction, two of whom had pre-existing **Parkinson**'s disease, and all of whom came from the medically ill consultation group. In each case the adverse effect resolved completely after discontinuation of the SSRI. The prevalence of SSRI-associated EPSE may be higher in the elderly, and in particular in medically ill patients with underlying brain disease.

L123 ANSWER 60 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1996:733885 Document No. 126:7829 Preparation of aromatic hydroxamic acid compounds for preventing and treating **neurodegenerative** diseases. Kato, Kaneyoshi; Miki, Shokyo; Naruo, Ken-Ichi; Takahashi, Hideki (Takeda Chemical Industries, Ltd., Japan). Eur. Pat. Appl. EP 737671 A2 19961016, 83 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1996-302494 19960410. PRIORITY: JP 1995-84342 19950410; JP 1995-215932 19950824.
AB The title compds. ArR1CHCH2QCONHOR2 (I) and ArR1C:CHQCONHOR2 [II; R1 = H, cyano, an optionally substituted hydrocarbon or Ph or naphthyl, NR3R4, acyl; R2 = acyl; R3, R4 = H, acyl, optionally substituted hydrocarbon group, or R3 and R4 may combine together with the adjacent N atom to form a ring; Ar = (un)substituted C6-14 aryl or 5-11 membered heteroaryl; Q = divalent C2-8 aliph. hydrocarbon group] or salts thereof are prepd. I and II (R2 = H, acyl) having excellent anti-**neurodegenerative** activity with a low cytotoxicity are useful for preventing or treating **neurodegenerative** diseases such as **Alzheimer**'s disease, **Parkinson**'s disease, Down's syndrome, Pick's disease, **multiple sclerosis**, and diseases typically mediated by viral infections, etc. Thus, 6-(4-methoxyphenyl)-6-(3-methyl-1,4-naphthoquinon-2-yl)hexanohydroxamic acid was reacted with Ac2O in the presence of pyridine to give I (R1 = 3-methyl-1,4-naphthoquinon-2-yl, Ar = 4-MePh, Q = (CH2)3, R2 = Ac). I (R1 = 3-methyl-1,4-naphthoquinon-2-yl, Ar = 4-MeOPh, Q = (CH2)3, R2 = H) showed IC50 of 0.08 .mu.M against lipopolysaccharides-induced NO prodn. in a mixed rat cerebral cell culture system.

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L123 ANSWER 61 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
96347663 EMBASE Document No.: 1996347663. Ondansetron: A review of its pharmacology and preliminary clinical findings in novel applications. Wilde M.I.; Markham A.. Adis International Limited, 41 Centorian Drive,Mairangi Bay, Auckland 10, New Zealand. Drugs 52/5 (773-794) 1996. ISSN: 0012-6667. CODEN: DRUGAY. Pub. Country: New Zealand. Language: English. Summary Language: English.

AB The use of odansetron, a selective serotonin 5-HT3 receptor antagonist, is well established in patients with nausea and vomiting associated with cancer chemotherapy, radiotherapy or anaesthesia and surgery. The wide distribution of 5-HT3 receptors in the body and the role of these receptors in disease have provided the rationale for investigation of ondansetron in novel applications. Preliminary data have shown odansetron to have clinical benefit in patients with nausea and vomiting associated with drug overdosage or poisoning, anti-infective or antidepressant therapies, uraemia or **neurological** trauma, and in patients with pruritus. Patients with gastrointestinal motility disorders (e.g., carcinoid syndrome, irritable bowel syndrome, diarrhoea associated with cryptosporidiosis or diabetes, and chronic refractory diarrhoea) have also shown some improvement when treated with ondansetron, as have patients with certain pain or CNS-related disorders [e.g., alcohol (ethanol) dependence, opiate withdrawal, vertigo, cerebellar tremor and **Parkinson**'s disease treatment-related psychosis]. In contrast to conventional antiemetics, odansetron is generally well tolerated with a lower incidence of sedation and only isolated case reports of extrapyrimidal reactions. Furthermore, unlike dopamine receptor-blocking neuroleptics, ondansetron does not appear to worsen the symptoms of **Parkinson**'s disease. Thus, in addition to its established indications, preliminary results suggest that ondansetron may be beneficial in a number of novel applications. This drug may represent a treatment alternative in patients with refractory disease, or an effective treatment of conditions for which current therapies are either poorly tolerated or not available. Further investigation of odansetron in a range of potential new applications appears to be warranted.

L123 ANSWER 62 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:348296 Document No.: PREV199699070652. Comparison of fluvoxamine versus amitriptyline for the treatment of depression in **Parkinson**'s disease. Rabey, Jose Martin (1); Orlov, E.; Korczyn, Amos D.. (1) Zerifin Israel. Neurology, (1996) Vol. 46, No. 2 SUPPL., pp. A374-A375. Meeting Info.: 48th Annual Meeting of the American Academy of Neurology San Francisco, California, USA March 23-30, 1996 ISSN: 0028-3878. Language: English.

L123 ANSWER 63 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:374441 Document No.: PREV199699096797. Serotonin syndrome and fluvoxamine in a **parkinsonian** patient. Le Cavorzin, P. (1); Sarkis, S. (1); Beneton, C.; Pinel, J. F. (1); Maruelle, L.; Le Vaou, P.; Allain, H.. (1) Serv. Neurologie, CHU Pontchaillou, rue Henri Le Guillou, 35043 Rennes France. Therapie (Paris), (1996) Vol. 51, No. 2, pp. 195-196. ISSN: 0040-5957. Language: French. Summary Language: French.

L123 ANSWER 64 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:338186 Document No.: PREV199699060542. Influence of fluvoxamine on tacrine metabolism in vitro: Potential implication for the hepatotoxicity in vivo. Becquemont, L. (1); Le Bot, M. A.; Riche, C.; Beaune, P.. (1) Laboratoire de Biochimie Pharmacologique, INSERM u 75, Faculte de Medecine Necker, 156 rue de Vaugirard, 75730 Paris Cedex 15 France. Fundamental & Clinical Pharmacology, (1996) Vol. 10, No. 2, pp. 156-157. ISSN: 0767-3981. Language: English.

Searched by: Mary Hale 308-4258 CM-1 1E01

L123 ANSWER 65 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
95282706 EMBASE Document No.: 1995282706. [Towards a treatment for dementias]. VERS UN TRAITEMENT DES DEMENCES. Ghika J.. Service de Neurologie, CHUV,1011 Lausanne, Switzerland. Schweizerische Rundschau fur Medizin/Praxis 84/38 (1050-1053) 1995.
ISSN: 0369-8394. CODEN: SRMPDJ. Pub. Country: Switzerland. Language: French. Summary Language: French; English; German.
AB The clinical manifestations of so-called 'untreatable dementias' result from neuronal dysfunction causing premature neuronal death. As long as the neurosciences won't have an explanation for the increased vulnerability and cause of death of neurons in **neurodegenerative** disorders, no preventive or curative treatment can be expected. So far, the treatment of dementia focuses essentially on the consequences of neuronal dysfunction or cell loss by either a palliative approach addressing psychosis, behavior or anxiety and depression, or by substitution of deficient neurotransmitters with quasi no success. Only tacrine, a cholinesterase inhibitor, now available in Switzerland, has a marginal effect in early cases, but every other substitutive approach has failed so far. Muscarinic agonists as well as antiamyloid substances will be tested soon in clinical trials. Growth factors (especially NGF) raise big hopes for the near future, but they are still under preclinical evaluation.

L123 ANSWER 66 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
95205484 EMBASE Document No.: 1995205484. Can an adjuvant treatment or a pharmacologic prevention be common to several diseases? The case of those associated to neuromediator defects. Mathe G.. Institut de Cancerologie/Immunologie, Hopital Suisse de Paris, 6 et 10 rue Minard,92130 Issy-les-Moulineaux, France. Biomedicine and Pharmacotherapy 49/4 (161-167) 1995.
ISSN: 0753-3322. CODEN: BIPHEX. Pub. Country: France. Language: English. Summary Language: English.
AB The author has tried to extrapolate on several **neurological** diseases of the ageing, Knoll's proposition to treat **Parkinson**'s disease chronically for relapse prevention, by MAO-B. At this occasion, the author makes a critical review of the clinical trial results concerning the new different series of depression treatments, as most authors propose today to use some new ones not only in depression, but in **Parkinson**'s and **Alzheimer**'s diseases and in ageing.

L123 ANSWER 67 OF 70 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
95282783 EMBASE Document No.: 1995282783. [Aggression: A bridge symptom between **neurology** and psychiatry]. AGGRESSIVITA: UN SINTOMO PONTE TRA **NEUROLOGIA** E PSICHIATRIA. Vitale R.. Universita degli Studi, VI Cattedra di Clinica Neurologica,Roma, Italy. Neurologia Psichiatria Scienze Umane 14/5 (745-770) 1994.
ISSN: 1120-2254. CODEN: NPSUEU. Pub. Country: Italy. Language: Italian. Summary Language: Italian; English.
AB Neuroanatomical, neurophysiological and neurotransmettitorial foundations playing a role in aggression are reevaluated until up-to-date contributions. Amygdala and serotonin seem to be respectively the outstanding responsible respectively neurophysiological and neurobiological basis of aggression. Epilepsy remains the best human model in spite of the fact that aggression in epilepsy is more a prejudice than a reality. Other **neurological** diseases to be considered are Huntington chorea and **Alzheimer**. Treatment is centered on Lithium carbonate and SSRI (Fluoxetine etc.). The phenomenon, considered its psychosocial implications, cannot be reduced to its biological foundations which are very important but playing a non-exclusive role like aggression in psychopathology (lacking of anatomical foundations) clearly

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demonstrates.

L123 ANSWER 68 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1995:182424 Document No.: PREV199598196724. Worsening of **Parkinsonism** with fluvoxamine: Two cases. Meco, Giuseppe (1); Bonifati, Vincenzo; Fabrizio, Edito; Vanacore, Nicola. (1) Dep. Neurosci., Viale dell'Universita 30, 00185 Roma Italy. Human Psychopharmacology, (1994) Vol. 9, No. 6, pp. 439-441. ISSN: 0885-6222. Language: English.
AB We describe two patients with **parkinsonism** and depressive symptoms who experienced a worsening of their motor disturbances following use of fluvoxamine, a serotonin selective reuptake inhibitor. The possible role of this drug in causing these adverse effects is discussed in the light of the complex serotonin-dopamine interactions in the brain.

L123 ANSWER 69 OF 70 HCAPLUS COPYRIGHT 2002 ACS
1991:558980 Document No. 115:158980 Preparation of aminopyridinylmethanols and aminomethylpyridinamines and related compounds as drugs. Effland, Richard Charles; Klein, Joseph Thomas (Hoechst-Roussel Pharmaceuticals, Inc., USA). Eur. Pat. Appl. EP 435222 A2 19910703, 37 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-125274 19901221. PRIORITY: US 1989-457610 19891227; US 1990-594497 19901009.
GI For diagram(s), see printed CA Issue.
AB The title compds. [I; R = OH, NH2, alkylamino, cycloalkylamino; R1 = H, alkyl, aralkyl, acyl, aroyl, etc.; R2 = H, alkyl, cycloalkyl, aryl, aralkyl; R3 = H, alkyl, cycloalkyl aralkyl, aryl; RR3 = O, NOH], useful as analgesics, antiinflammatory agents, and for treating such memory dysfunctions as **Alzheimer**'s disease, are prepd. To a cooled soln. of 8 g aldehyde II in THF was added 3.0M MeMgBr in Et2O, the mixt. was stirred with NH4Cl, and extd. with Et2O to give 4.5 g I (R = OH, R1 = Me3CCO, R2 = H, R3 = Me), which showed 89% inhibition of phenylquinone-induced writhing in mice at 20 mg/kg s.c.

L123 ANSWER 70 OF 70 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1993:128393 Document No.: PREV199344059393. Fluvoxamine, a novel 5-hydroxytryptamine uptake inhibitor: Present and future clinical applications. Altamura, A. C.; Mauri, M. C.; Moro, A. R.. Inst. Clinical Psychiatry, Univ. Milan, Lab. Clinical Neuropsychopharmacology, Policlinico, Guardia 2, 20122 Milan Italy. Nappi, G. [Editor]; Bono, G. [Editor]; Sandrini, G. [Editor]; Martignoni, E. [Editor]; Micieli, G. [Editor]. (1991) pp. 273-279. Headache and depression: Serotonin pathways as a common clue. Publisher: Raven Press 1185 Avenue of the Americas, New York, New York 10036-2806, USA. ISBN: 0-88167-861-9. Language: English.

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Searched by: Mary Hale 308-4258 CM-1 1E01

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L10 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:46416 CAPLUS
DOCUMENT NUMBER: 130:89983
TITLE: New indications for thalidomide
AUTHOR(S): De Jong-van den Berg, L. T. W.; Rutgers, J.; Cornel, M. C.; Takx-Koehlen, B. C. M. J.
CORPORATE SOURCE: Groningen Inst. Drug Studies, Rijksuniv. Groningen, Groningen, 9713 AW, Neth.
SOURCE: Ziekenhuisfarmacie (1998), 14(4), 190-193
CODEN: ZIFAEM; ISSN: 0169-2720
PUBLISHER: Nederlandse Vereniging van Ziekenhuisapothekers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Dutch
AB A brief review with 38 refs. is given on new indications for thalidomide. Besides the beneficial effects of thalidomide in **erythema nodosum leprosy** the drug is efficacious in other major disorders such as aphthae and ulcers in aids, tuberculosis, autoimmune diseases, and tumors.

=>

=>
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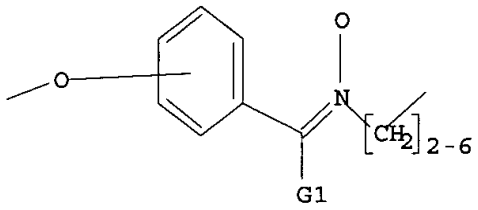
L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS
L1 STR



G1 H,Me,Et,n-Pr,n-Bu

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 16:56:20 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 151 TO ITERATE
100.0% PROCESSED 151 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2283 TO 3757
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 16:56:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3122 TO ITERATE
100.0% PROCESSED 3122 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=> s nitrone

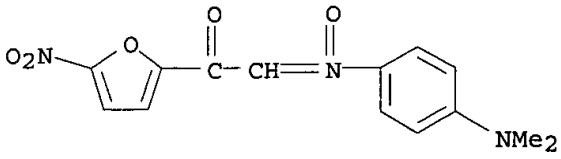
L4 1059 NITRONE

=> s l4 and 1-2/nr

5825234 1-2/NR
L5 720 L4 AND 1-2/NR

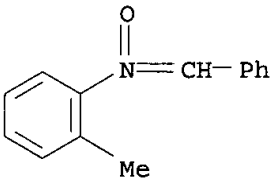
=> d scan

L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, N-[p-(dimethylamino)phenyl]-.alpha.-(5-nitro-2-furoyl)-(7CI)**
MF C14 H13 N3 O5

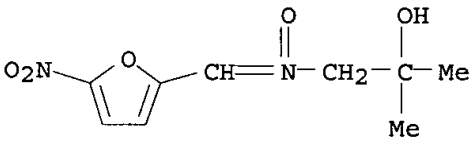


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

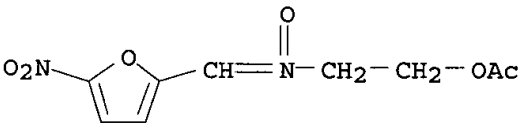
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN Benzenamine, 2-methyl-N-(phenylmethylene)-, N-oxide (9CI)
MF C14 H13 N O



L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, N-(2-hydroxy-2-methylpropyl)-.alpha.-(5-nitro-2-furyl)-(8CI)**
MF C9 H12 N2 O5

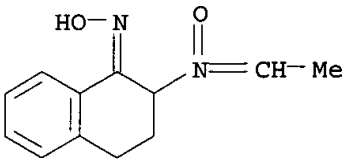


L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, N-(2-hydroxyethyl)-.alpha.-(5-nitro-2-furyl)-, acetate (ester) (8CI)**
MF C9 H10 N2 O6

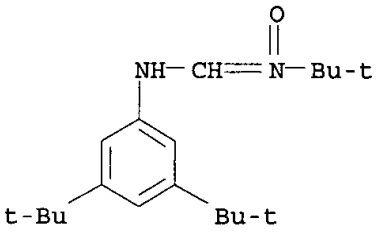


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

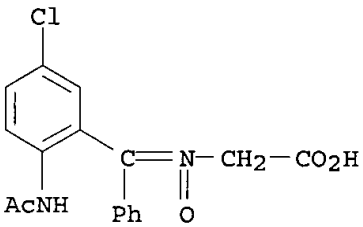
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, .alpha.-methyl-N-(1,2,3,4-tetrahydro-1-oxo-2-naphthyl)-, oxime (8CI)**
MF C12 H14 N2 O2



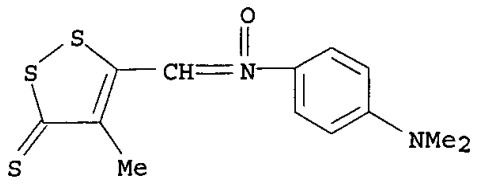
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, N-tert-butyl-.alpha.-(3,5-di-tert-butylanilino)- (8CI)**
MF C19 H32 N2 O



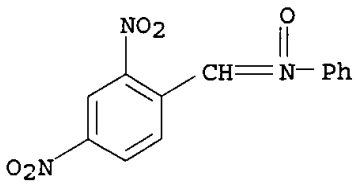
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, .alpha.-(2-acetamido-5-chlorophenyl)-N-(carboxymethyl)-.alpha.-phenyl- (7CI, 8CI)**
MF C17 H15 Cl N2 O4



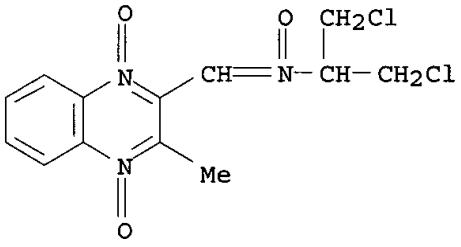
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, N-(p-dimethylaminophenyl)-.alpha.-(4-methyl-3-thioxo-1,2-dithiol-5-yl)- (6CI)**
MF C13 H14 N2 O S3



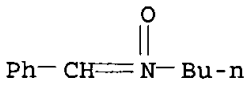
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN Benzenamine, N-[(2,4-dinitrophenyl)methylene]-, N-oxide (9CI)
MF C13 H9 N3 O5



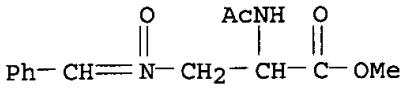
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 2-Propanamine, 1,3-dichloro-N-[(3-methyl-1,4-dioxido-2-quinoxalinyl)methylene]-, N-oxide (9CI)
MF C13 H13 Cl2 N3 O3



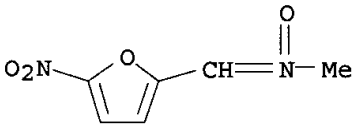
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 1-Butanamine, N-(phenylmethylene)-, N-oxide (9CI)
MF C11 H15 N O



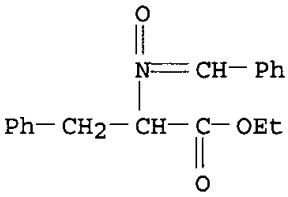
L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN Alanine, N-acetyl-3-[oxido(phenylmethylene)amino]-, methyl ester (9CI)
MF C13 H16 N2 O4



L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN Methanamine, N-[(5-nitro-2-furanyl)methylene]-, N-oxide (9CI)
MF C6 H6 N2 O4



L5 720 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **Nitrone, N-(.alpha.-carboxyphenethyl)-.alpha.-phenyl-, ethyl ester (8CI)**
MF C18 H19 N O3



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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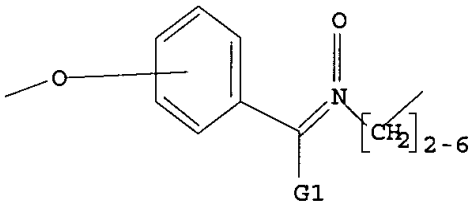
Uploading 09172763.str

L6 STRUCTURE UPLOADED

=> d

L6 HAS NO ANSWERS
L6 STR



G1 H,Me,Et,n-Pr,n-Bu

Structure attributes must be viewed using STN Express query preparation.

=> s l6

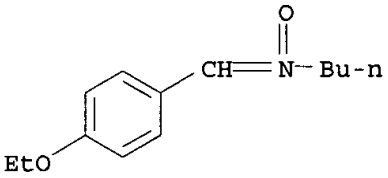
SAMPLE SEARCH INITIATED 16:59:15 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 151 TO ITERATE
100.0% PROCESSED 151 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2283 TO 3757
PROJECTED ANSWERS: 1 TO 80

L7 1 SEA SSS SAM L6

=> d

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1999 ACS
RN 223650-08-6 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS 3D CONCORD
MF C13 H19 N O2
SR CA
LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

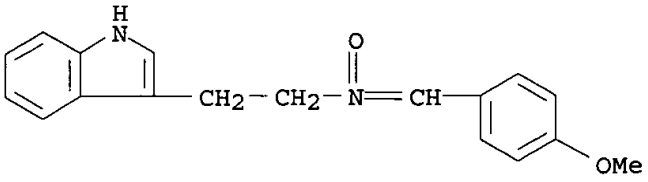
=> s l6 full

FULL SEARCH INITIATED 16:59:27 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3122 TO ITERATE
100.0% PROCESSED 3122 ITERATIONS 26 ANSWERS
SEARCH TIME: 00.00.01

L8 26 SEA SSS FUL L6

=> d scan

L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 1H-Indole-3-ethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI)
MF C18 H18 N2 O2



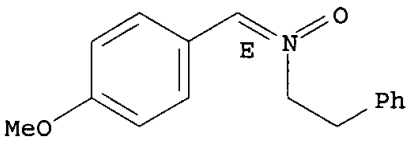
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1-

'1-' IS NOT VALID HERE

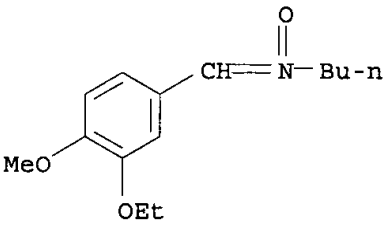
To display more answers, enter the number of answers you would like to see. To end the display, enter "NONE", "N", "0", or "END".
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN Benzeneethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (E)- (9CI)
MF C16 H17 N O2

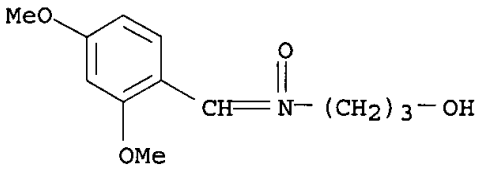
Double bond geometry as shown.



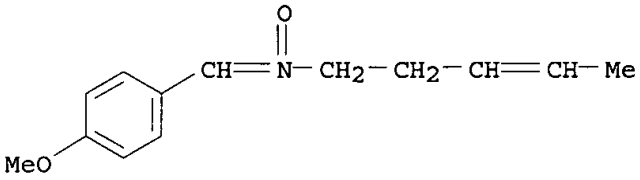
L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C14 H21 N O3



L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 1-Propanol, 3-[[(2,4-dimethoxyphenyl)methylene]oxidoamino]- (9CI)
MF C12 H17 N O4

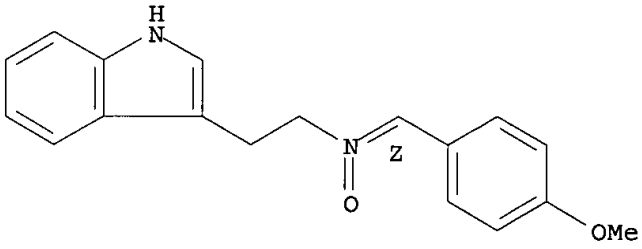


L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 3-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z,E)- (9CI)
MF C13 H17 N O2

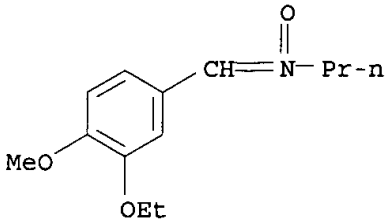


L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 1H-Indole-3-ethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)-(9CI)
MF C18 H18 N2 O2

Double bond geometry as shown.



L8 26 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C13 H19 N O3



=> s l8 full

L9 12 L8

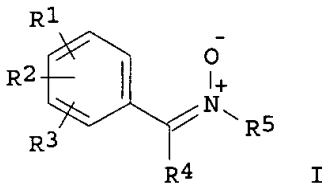
=> d ibib abs hitstr 1-12

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:282195 CAPLUS
DOCUMENT NUMBER: 130:311617
TITLE: Preparation of .alpha.-aryl-N-alkylnitrones for treatment of neurodegenerative, autoimmune, and inflammatory disease and as analytical reagents for detection of free radicals.
INVENTOR(S): Kelleher, Judith A.; Maples, Kirk R.; Dykman, Alina; Zhang, Yong-Kang; Wilcox, Allan L.; Levell, Julian
PATENT ASSIGNEE(S): Centaur Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920601	A1	19990429	WO 98-US21624	19981016

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 97-62324 19971017
US 97-63736 19971029
US 98-90475 19980624
OTHER SOURCE(S): MARPAT 130:311617
GI

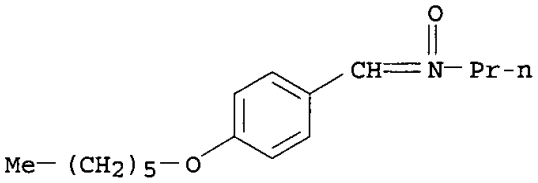


I

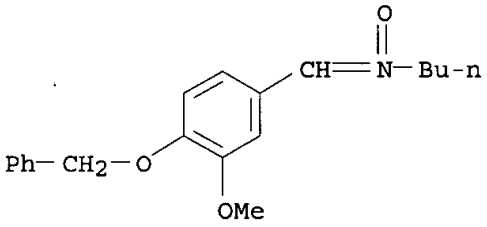
AB Title compds. [I; R1 = alkoxy, alkaryloxy, alkcycloalkoxy, aryloxy, cycloalkoxy; R2 = H, alkoxy, alkcycloalkoxy, cycloalkoxy, halo; adjacent R1R2 = alkylenedioxy; R3 = H, alkoxy, alkcycloalkoxy, cycloalkoxy, halo; R4 = H, alkyl; R5 = (substituted) alkyl, cycloalkyl; with provisos], were prepd. Thus, 4-hydroxybenzaldehyde was refluxed 30 min. with NaOH in EtOH; I(CH2)5CH3 was added and the mixt. was refluxed 68 h to give a residue which was kept 18 h with PrNO2, NH4Cl, and Zn in EtOH/H2O to give 12.4% .alpha.-4-hexyloxyphenyl-N-propylnitrone. Several I at 100 mg/kg orally in rats treated with M. tuberculin in incomplete Freunds adjuvant reduced CNS inflammatory deficit.

IT **223649-61-4P 223649-84-1P 223649-85-2P**
223649-86-3P 223649-87-4P 223650-08-6P
223650-16-6P 223650-17-7P 223650-39-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-aryl-N-alkylnitrones for treatment of neurodegenerative, autoimmune, and inflammatory disease and as anal. reagents for detection of free radicals)

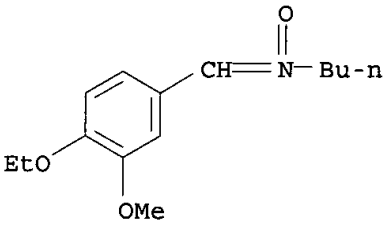
RN 223649-61-4 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



RN 223649-84-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



RN 223649-85-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



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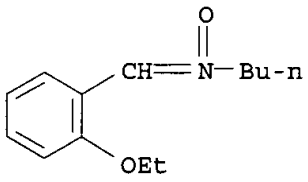

RN 223649-87-4 CAPLUS
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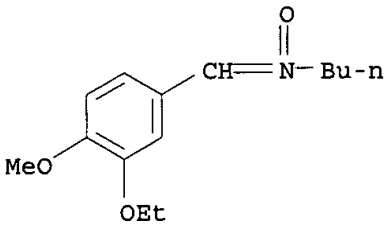
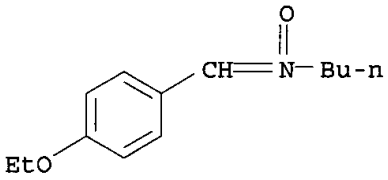
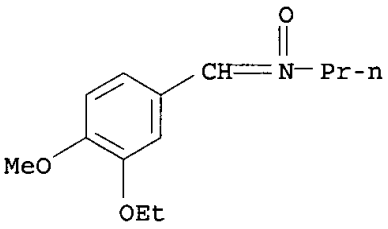


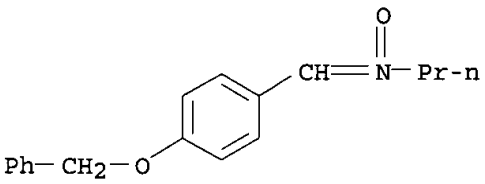
RN 223650-08-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



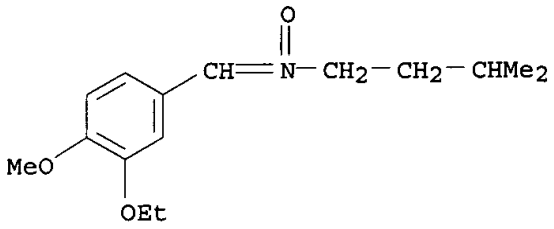
RN 223650-16-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



RN 223650-17-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



RN 223650-39-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

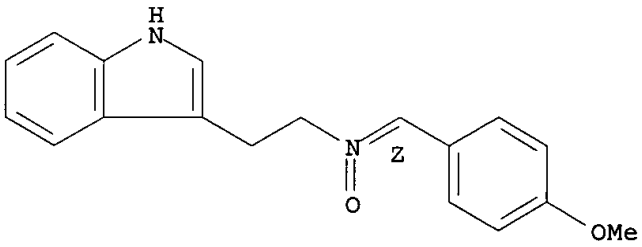


L9 ANSWER 2 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:532121 CAPLUS
DOCUMENT NUMBER: 129:289717
TITLE: Chiral Lewis Acid-Mediated Enantioselective Pictet-Spengler Reaction of Nb-Hydroxytryptamine with Aldehydes
AUTHOR(S): Yamada, Hideki; Kawate, Tomohiko; Matsumizu, Miyako; Nishida, Atsushi; Yamaguchi, Kentaro; Nakagawa, Masako
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences and Chemical Analytical Center, Chiba University, Chiba, 263-8522, Japan
SOURCE: J. Org. Chem. (1998), 63(18), 6348-6354
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:289717

AB The first example of a reagent-controlled enantioselective Pictet-Spengler reaction is demonstrated. Using diisopinocampheylchloroborane as a chiral Lewis acid catalyst, the Pictet-Spengler reaction of Nb-hydroxytryptamine with aldehydes gave the corresponding 2-hydroxytetrahydro-.beta.-carbolines in up to 90% ee. The enantioselective Pictet-Spengler reaction catalyzed by chiral binaphthol-derived Bronsted acid-assisted Lewis acids, with up to 91% ee, is also demonstrated.

IT **213841-85-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(chiral Lewis acid-mediated stereoselective Pictet-Spengler reaction of N-hydroxytryptamine with aldehydes)
RN 213841-85-1 CAPLUS
CN 1H-Indole-3-ethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:522216 CAPLUS
DOCUMENT NUMBER: 127:248038
TITLE: Enantioselective Pictet-Spengler reaction of nitrones derived from Nb-hydroxytryptamine and aldehydes

catalyzed by chiral Bronsted acid-assisted Lewis acids

AUTHOR(S): Kawate, Tomohiko; Yamada, Hideki; Matsumizu, Miyako; Nishida, Atsushi; Nakagawa, Masako

CORPORATE SOURCE: Faculty Pharmaceutical Sciences, Chiba University, Chiba, 263, Japan

SOURCE: Synlett (1997), (7), 761-762
CODEN: SYNLES; ISSN: 0936-5214

PUBLISHER: Thieme

DOCUMENT TYPE: Journal

LANGUAGE: English

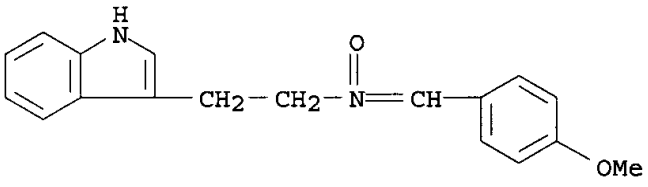
OTHER SOURCE(S): CASREACT 127:248038

AB The enantioselective Pictet-Spengler reaction catalyzed by chiral binaphthol-derived Bronsted acid-assisted Lewis acids is demonstrated. The Pictet-Spengler reaction of nitrones prepd. from Nb-hydroxytryptamine and aldehydes gave the corresponding 1-substituted 2-hydroxytetrahydro-.beta.-carbolines with .ltoreq.91% ee.

IT **98664-53-0**
RL: RCT (Reactant)
(stereoselective Pictet-Spengler reaction of nitrones catalyzed by Bronsted acid-assisted Lewis acids)

RN 98664-53-0 CAPLUS

CN 1H-Indole-3-ethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:344341 CAPLUS

DOCUMENT NUMBER: 125:86597

TITLE: Enantioselective asymmetric Pictet-Spengler reaction catalyzed by diisopinocampheylchloroborane

AUTHOR(S): Kawate, Tomohiko; Yamada, Hideki; Soe, Than; Nakagawa, Masako

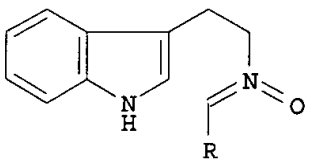
CORPORATE SOURCE: Faculty Pharmaceutical Sci., Chiba Univ., Chiba, 263, Japan

SOURCE: Tetrahedron: Asymmetry (1996), 7(5), 1249-1252
CODEN: TASYE3; ISSN: 0957-4166

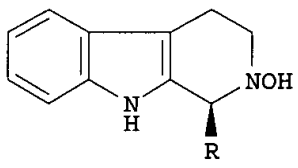
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



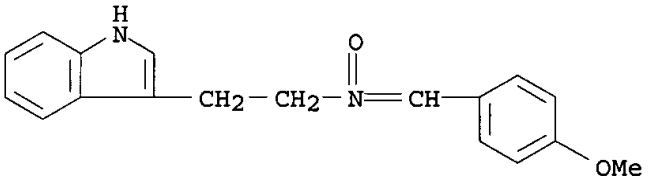
II

AB The first example of a reagent-controlled enantioselective Pictet-Spengler reaction was demonstrated. Nitrones I (R = Ph, alkyl) were prepd. from aldehydes and Nb-hydroxytryptamine. Employing diisopinocampheylchloroborane as a chiral Lewis acid catalyst, the Pictet-Spengler reaction of I gave the 2-hydroxy-tetrahydro-.beta.-carbolines II (same R) with up to 90% enantiomeric excess. For example, the (+)-DIP chloride-catalyzed Pictet-Spengler reaction of N-(phenylmethylene)-1H-indole-3-ethanamine N-oxide gave (S)-2,3,4,9-tetrahydro-2-hydroxy-1-phenyl-1H-pyrido[3,4-b]indole. On the other hand, the (-)-DIP chloride-catalyzed Pictet-Spengler reaction (R)-2,3,4,9-tetrahydro-2-hydroxy-1-phenyl-1H-pyrido[3,4-b]indole.

IT **98664-53-0**
RL: RCT (Reactant)
(diisopinocampheylborane-catalyzed Pictet-Spengler reaction of indoleethanamine derivs.)

RN 98664-53-0 CAPLUS

CN 1H-Indole-3-ethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:258379 CAPLUS

DOCUMENT NUMBER: 122:160227

TITLE: Synthesis and separation of the E and Z isomers of simple aldonitrones

AUTHOR(S): Sivasubramanian, Shanmugaperumal; Mohan, Ponnusamy; Thirumalaikumar, Muniappan; Muthusubramanian, Shanmugan

CORPORATE SOURCE: Dep. Org. Chem., Madurai Kamaraj Univ., Madurai, 625 021, India

SOURCE: J. Chem. Soc., Perkin Trans. 1 (1994), (23), 3353-4
CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 122:160227

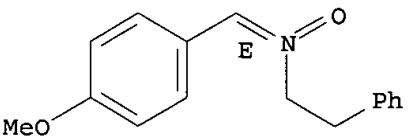
AB The uncommon E isomer of simple aldonitrones has been obtained in significant amts. for the first time in the case of .alpha.-phenyl-N-(.beta.-phenylethyl)nitrones.

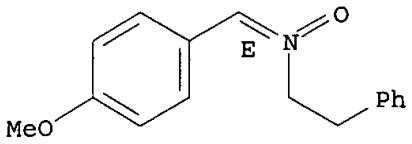
IT **161325-26-4P 161325-27-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sepn. of the E and Z isomers of simple aldonitrones and isomerization and)

RN 161325-26-4 CAPLUS

CN Benzeneethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (E)- (9CI) (CA INDEX NAME)

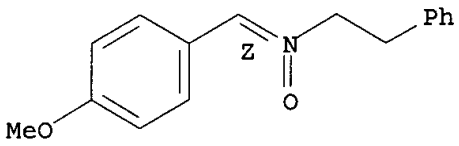
Double bond geometry as shown.



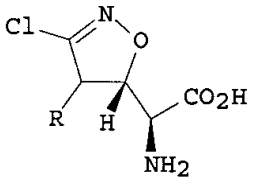


RN 161325-27-5 CAPLUS
CN Benzeneethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1993:35602 CAPLUS
DOCUMENT NUMBER: 118:35602
TITLE: Biosynthesis of acivicin. 3. Incorporation of ornithine and N.delta.-hydroxyornithine
AUTHOR(S): Gould, Steven J.; Ju, Shyhchen
CORPORATE SOURCE: Dep. Chem., Oregon State Univ., Corvallis, OR, 97331, USA
SOURCE: J. Am. Chem. Soc. (1992), 114(26), 10166-72
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=H
II, R=OH

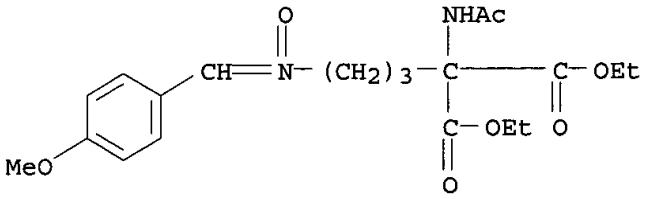
AB The biosynthesis of the antibiotics acivicin (I) and 4-hydroxyacivicin (II) was studied in Streptomyces sviceus. Initial expts. identified ornithine as the primary precursor, rather than glutamic acid or glutamine. Incorporation of [5-13C,15N]ornithine established the retention of the .omega.-amino N. Incorporation of [2,3,3-2H3]-, [3,3,4,4-2H4]-, [3R-2H]-, and [3S-2H]ornithines revealed the complete loss of H-2, replacement of the 3S H with the isoxazoline O, and partial loss of the 3R H. Incorporation of 18O2 revealed the derivation of the isoxazoline O and the 4-OH group of II from O2, although partial exchange of the former had occurred. N.delta.-Hydroxyornithine (III), rather than either erythro- or threo-.beta.-hydroxyornithine, is the 1st committed intermediate in the pathway. [14C-I was metabolized to [14C]-II, but the reverse did not occur. A linear pathway from ornithine through III to I

and then to II is proposed to account for these findings.

IT **144811-53-0P 144811-55-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

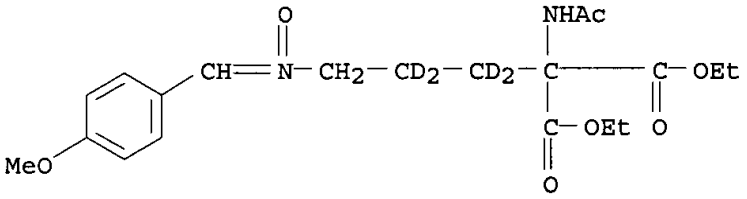
RN 144811-53-0 CAPLUS

CN Propanedioic acid, (acetylamino)[3-[[(4-methoxyphenyl)methylene]oxidoamino]propyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 144811-55-2 CAPLUS

CN Propanedioic acid, (acetylamino)[3-[[(4-methoxyphenyl)methylene]oxidoamino]propyl-1,1,2,2-d4]-, diethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1990:158107 CAPLUS

DOCUMENT NUMBER: 112:158107

TITLE: Studies on intramolecular 1,3-dipolar cycloaddition reactions. III. The synthesis of a novel heterocyclic ring system by regiospecific cycloaddition

AUTHOR(S): Chen, Qinghua; Yu, Xiuzhi; Zhang, Tieyuan; Jia, Xibei

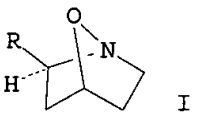
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China

SOURCE: Acta Chim. Sin. (Engl. Ed.) (1989), (2), 176-82
CODEN: ACSIEW

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB RCH:N(O)CH2CH2CH:CH2 [I; R = (un)substituted phenyl, 2-furyl, 2-thienyl, pyrrol-2-yl] were prepd. in 43-70% yield by reaction of (Z)-RCH:NOH with

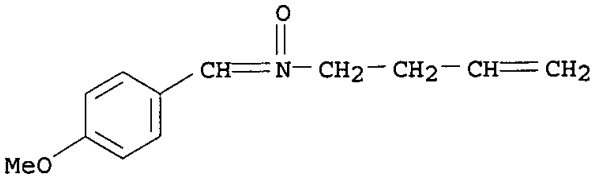
BrCH2CH2CH:CH2 in EtONa/EtOH.

IT **126088-30-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and intramol. cycloaddn. reaction of)

RN 126088-30-0 CAPLUS

CN 3-Buten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)- (9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1989:533451 CAPLUS

DOCUMENT NUMBER: 111:133451

TITLE: Intramolecular 1,3-dipolar cycloaddition reactions. IV. Thermochemical and photochemical reactions of some 1,3-dipolar nitrone systems and their regioselectivities

AUTHOR(S): Chen, Qinghua; Xie, Mengxia; Jia, Xibei; Wang, Xueliang

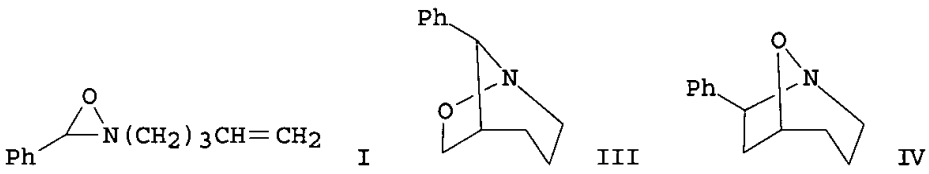
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China

SOURCE: Youji Huaxue (1989), 9(2), 156-62
CODEN: YCHHDX; ISSN: 0253-2786

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



I III IV

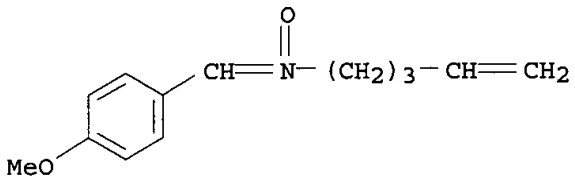
AB The substituent effects on the reactivities and the regioselectivities of the title reactions were examd. by chromatog. methods. On irradn. by a Hg lamp at .lambda. .gtoreq.302 nm, nitrones, e.g., CHPh:N(O)(CH2)3CH:CH2, gave oxaziridine I. I rearranged further to BzNH(CH2)3CH:CH2 (II) at .lambda. .gtoreq.270 nm. Upon heating, II was transformed back to the nitrone and subsequently cyclized to give III and IV.

IT **122753-93-9**

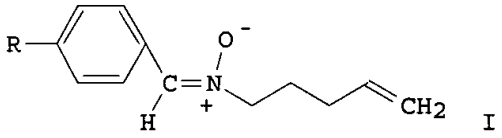
RL: RCT (Reactant)
(photolysis of)

RN 122753-93-9 CAPLUS

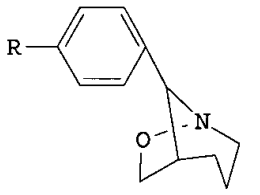
CN 4-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



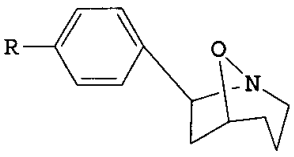
L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1987:515572 CAPLUS
DOCUMENT NUMBER: 107:115572
TITLE: Intramolecular 1,3-dipolar cycloaddition reactions. I. Thermochemical reactivities and regioselectivities of 4-substituted phenyl(N-4-pentenyl)nitrones
AUTHOR(S): Chen, Qinghua; Meng, Min
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China
SOURCE: Huaxue Xuebao (1986), 44(9), 927-33
CODEN: HHHPA4; ISSN: 0567-7351
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 107:115572
GI



I

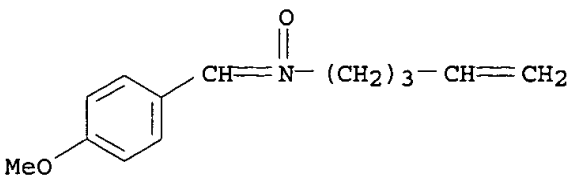


VI

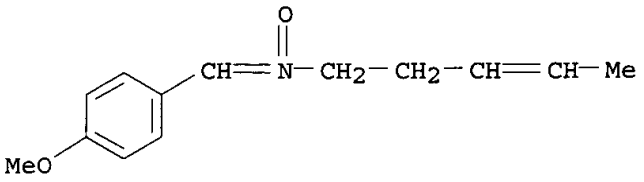


VII

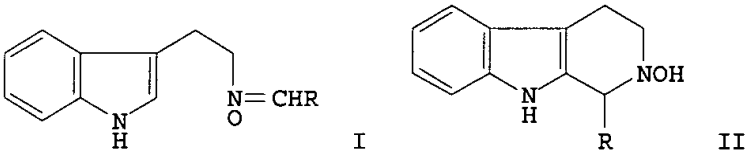
AB Refluxing nitrones I [R = NO2 (II), Br (III), H (IV), MeO (V)] in toluene for 24 h gave 54-80% cycloadducts VI and VII (VI/VII = 2). The thermochem. reactivity is in the order of II > III > IV > V.
IT **109830-20-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cycloaddn. reaction of)
RN 109830-20-8 CAPLUS
CN 4-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)- (9CI) (CA INDEX NAME)



IT **109830-28-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 109830-28-6 CAPLUS
CN 3-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z,E)- (9CI)
(CA INDEX NAME)



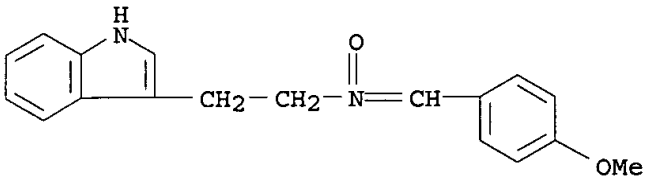
L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1985:560749 CAPLUS
DOCUMENT NUMBER: 103:160749
TITLE: Synthesis of N(2)-hydroxy-1,2,3,4-tetrahydro-.beta.-carbolines
AUTHOR(S): Han, So Yeop; Lakshmikantham, M. V.; Cava, Michael P.
CORPORATE SOURCE: Dep. Chem., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Heterocycles (1985), 23(7), 1671-3
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:160749
GI



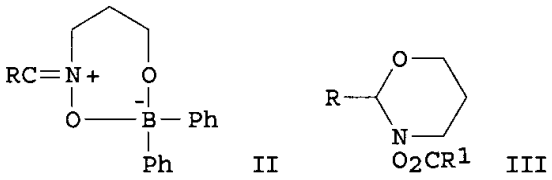
I II

AB N-Hydroxytryptamine condensed readily with a series of aldehydes in the presence of a catalytic amt. of AcOH to give the corresponding nitrones I (R = Me, Et, Pr, p-MeOC6H4, p-ClC6H4, o-BrC6H4), which in turn were cyclized by HCl to the stable N(2)-hydroxytetrahydro-.beta.-carbolines (II). .beta.-Carbolines of this type have not previously been synthesized, and are of interest because of their structural relationship to several potent antiviral marine alkaloids (eudistomins C, E, K and L).

IT **98664-53-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and intramol. cyclization of, hydroxytetrahydrocarboline deriv. from)
RN 98664-53-0 CAPLUS
CN 1H-Indole-3-ethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI)
(CA INDEX NAME)



L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1984:138667 CAPLUS
DOCUMENT NUMBER: 100:138667
TITLE: Ring-chain isomerism of N-(3-hydroxyalkyl)nitrones. I. C-Aryl-N-(3-hydroxypropyl)nitrones
AUTHOR(S): Kliegel, Wolfgang; Preu, Lutz
CORPORATE SOURCE: Inst. Pharm. Chem., Tech. Univ. Braunschweig, Braunschweig, D-3300, Fed. Rep. Ger.
SOURCE: Liebigs Ann. Chem. (1983), (11), 1937-49
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: German
GI

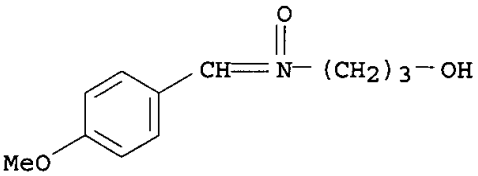


II III

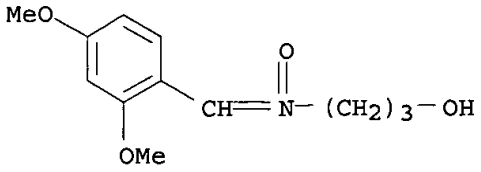
AB RHC:N+(O-)(CH2)3OH [I, R = Ph, p-O2NC6H4, 4-ClC6H4, 4-MeOC6H4, 2,4-(MeO)2C6H3, p-Me2NC6H4, 3,4-MeO(HO)C6H3] were prepd. by oxidn. of PhCH:N(CH2)3OH with AcOOH followed by hydrolysis and condensation of the 3-(hydroxyamino)propanol with RCHO. The isomerization of I and perhydro-1,3-oxazines was shown by the formation of diphenylboron chelates II and acyloxyperhydrooxazines III (R1 = Ph, p-O2NC6H4).

IT **88690-68-0P 88690-69-1P 88707-61-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ring-chain isomerization of)

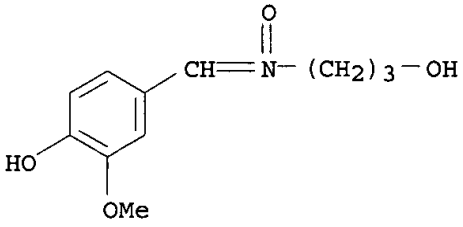
RN 88690-68-0 CAPLUS
CN 1-Propanol, 3-[[(4-methoxyphenyl)methylene]oxidoamino]- (9CI) (CA INDEX NAME)



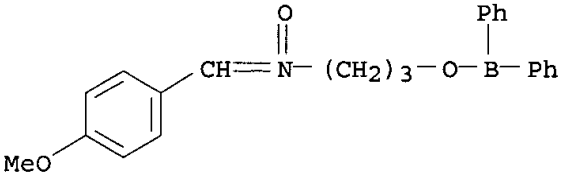
RN 88690-69-1 CAPLUS
CN 1-Propanol, 3-[[(2,4-dimethoxyphenyl)methylene]oxidoamino]- (9CI) (CA INDEX NAME)



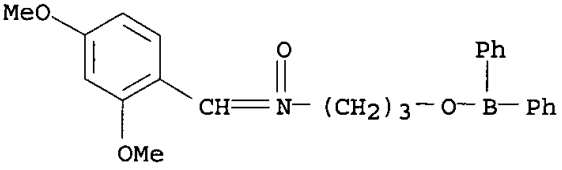
RN 88707-61-3 CAPLUS
CN Phenol, 4-[[(3-hydroxypropyl)oxidoimino]methyl]-2-methoxy- (9CI) (CA INDEX NAME)



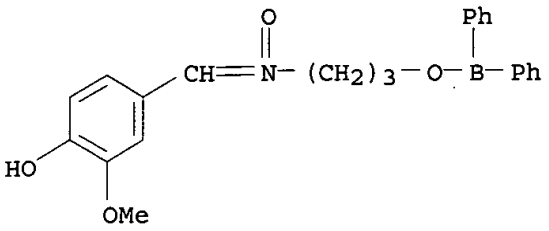
IT **88690-73-7P 88690-74-8P 88690-76-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 88690-73-7 CAPLUS
CN Borinic acid, diphenyl-, 3-[[(4-methoxyphenyl)methylene]oxidoamino]propyl ester (9CI) (CA INDEX NAME)



RN 88690-74-8 CAPLUS
CN Borinic acid, diphenyl-, 3-[[(2,4-dimethoxyphenyl)methylene]oxidoamino]propyl ester (9CI) (CA INDEX NAME)

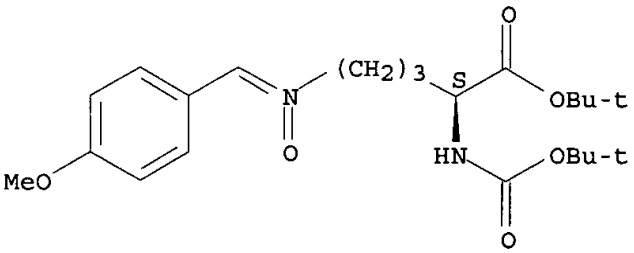


RN 88690-76-0 CAPLUS
CN Borinic acid, diphenyl-, 3-[[(4-hydroxy-3-methoxyphenyl)methylene]amino]oxidopropyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1974:437798 CAPLUS
DOCUMENT NUMBER: 81:37798
TITLE: Metabolic products of microorganisms. 130. Synthesis of .delta.-N-hydroxy-L-arginines
AUTHOR(S): Widmer, Joerg; Keller-Schierlein, Walter
CORPORATE SOURCE: Org.-Chem. Lab., Eidg. Tech. Hochsch., Zurich, Switz.
SOURCE: Helv. Chim. Acta (1974), 57(3), 657-64
CODEN: HCACAV
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB .delta.-N-Hydroxy-L-arginine (I) was prepd. by converting RNH(CH2)3CH(NHR1)CO2R2 (II, R = PhCH2O2C, R1 = R2 =H) to its tert-Bu ester, protecting the N with Me3CO2CN3, hydrolyzing, and treating the II (R = H, R1 = CO2CMe3, R2 = CMe3) with p-MeOC6H4CHO. The p-MeOC6H4CH:N(CH2)3CH(NHCO2CMe3)CO2CMe3 was oxidized to the oxaziridine III, hydrolyzed to II (R = OH, R1 = CO2CMe3, R2 = CMe3), treated with H2NC(SEt):NH and protective groups cleaved with CF3CO2H to give I. Hydrolysis of III also gave pmeOC6H4CH :-N(O)(CH2)3CH(NHCO2CMe3)CO2CMe3, which was hydrolyzed with 6N HCl to II (R = OH, R1 = R2 = H). Synthetic I had the same antibiotic activity as natural I.
IT **53123-09-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)
RN 53123-09-4 CAPLUS
CN L-Ornithine, N2-[(1,1-dimethylethoxy)carbonyl]-N5-[(4-methoxyphenyl)methylene]-, 1,1-dimethylethyl ester, N5-oxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



=> file beilstein

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	47.06	297.76

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -6.43      -6.43

FILE 'BEILSTEIN' ENTERED AT 17:04:06 ON 06 JUN 1999
COPYRIGHT (c) 1999 Beilstein Chemiedaten und Software GmbH, Beilstein Institut fuer
Literatur der organischen Chemie

FILE LAST UPDATED: 1 MAR 1999

FILE COVERS 1779 TO 1999.
*** CAS REGISTRY NUMBERS FOR 4,356,237 SUBSTANCES AVAILABLE ***
*** FILE CONTAINS 7,446,355 SUBSTANCES ***

**********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.                *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE   *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE          *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                        *
* FOR PRICE INFORMATION SEE HELP COST                                *
**********************************************************************



=> d his


     (FILE 'HOME' ENTERED AT 16:55:54 ON 06 JUN 1999)

     FILE 'REGISTRY' ENTERED AT 16:56:01 ON 06 JUN 1999
L1              STRUCTURE UPLOADED
L2            0 S L1
L3            0 S L1 FULL
L4         1059 S NITRONE
L5          720 S L4 AND 1-2/NR
L6              STRUCTURE UPLOADED
L7            1 S L6
L8           26 S L6 FULL

     FILE 'CAPLUS' ENTERED AT 17:00:12 ON 06 JUN 1999
L9           12 S L8 FULL

     FILE 'BEILSTEIN' ENTERED AT 17:04:06 ON 06 JUN 1999

=> s l7 full

L10           0 L7

=> d l7

YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y



L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 1999 ACS
RN   223650-08-6  REGISTRY
CN   INDEX NAME NOT YET ASSIGNED
FS   3D CONCORD
MF   C13 H19 N O2
SR   CA
LC   STN Files:   CA, CAPLUS
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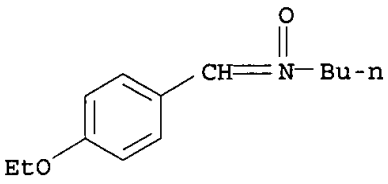
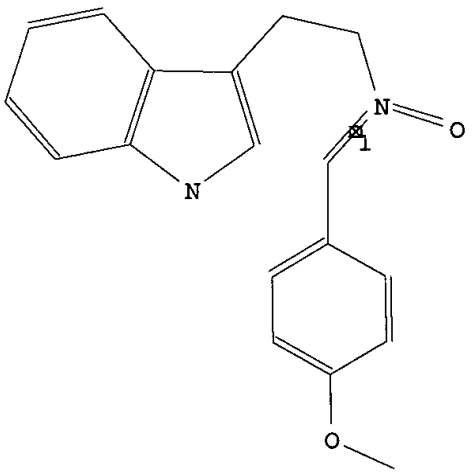


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
=> s l6 full

FULL SEARCH INITIATED 17:05:02 FILE 'BEILSTEIN'
FULL SCREEN SEARCH COMPLETED -   1914 TO ITERATE
 95.4% PROCESSED    1825 ITERATIONS                          12 ANSWERS
100.0% PROCESSED    1914 ITERATIONS                          13 ANSWERS
SEARCH TIME: 00.00.21

L11          13 SEA SSS FUL L6

=> d hid

'HID' IS NOT A VALID FORMAT FOR FILE 'BEILSTEIN'

The following are valid formats:

QRD --------- Query Related Data (IDE plus HIT)
IDE --------- Identification of Substance, plus Structure
  (BRN, MF, LSF, CN, SY, AUN, FW, SO, NTE, LN, RN, BPR, RSI, OS, STR)
GEN --------- General Data
ALL --------- All Display fields (Lengthy display!)
CHE --------- Chemical Data
PHY --------- Physical Data
HIT --------- All fields containing hit terms
Hit terms will be highlighted in all IDE fields in the BEILSTEIN file
A maximum of 20 values are displayed in each single property field.
Use DISPLAY F<prop> for FULL format, e.g. FBP instead of BP.
For more information about display formats, and how to display
individual selected properties, enter 'HELP FORMAT' at an arrow
prompt, e.g. => HELP FORMAT.
ENTER DISPLAY FORMAT (QRD):end


=> d his


     (FILE 'HOME' ENTERED AT 16:55:54 ON 06 JUN 1999)

     FILE 'REGISTRY' ENTERED AT 16:56:01 ON 06 JUN 1999
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           0 S L1 FULL
L4        1059 S NITRONE
L5         720 S L4 AND 1-2/NR
L6             STRUCTURE UPLOADED
L7           1 S L6
L8          26 S L6 FULL

     FILE 'CAPLUS' ENTERED AT 17:00:12 ON 06 JUN 1999
L9           12 S L8 FULL

     FILE 'BEILSTEIN' ENTERED AT 17:04:06 ON 06 JUN 1999
```

```
L10             0 S L7 FULL

     FILE 'REGISTRY' ENTERED AT 17:04:42 ON 06 JUN 1999

     FILE 'BEILSTEIN' ENTERED AT 17:04:43 ON 06 JUN 1999
L11            13 S L6 FULL

=> s l11 not l8

               4 L8
L12            9 L11 NOT L8

=> d ide


L12  ANSWER 1 OF 9  BEILSTEIN  COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN):    7819581  Beilstein
Molecular Formula (MF):      C18 H18 N2 O2
Beilstein Reference (SO):    6-22
General Comments (NTE):      Stereo compound; Referenced by other compounds
Rltd. Stereoisomers (RSI):   6419321
Formula Weight (FW):         294.35
Lawson Number (LN):          27897; 8629; 289
```




```
    Atom/Bond Notes:
        1. CIP Descriptor: Z

=> 0

0 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l12 and 1/n

       1783601 1/N
L13            3 L12 AND 1/N

=> d ide
```

L13 ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 7077777 Beilstein
Molecular Formula (MF): **C16 H17 N O2**
Beilstein Reference (SO): 6-15
General Comments (NTE): Stereo compound
Rltd. Stereoisomers (RSI): 7077776
Formula Weight (FW): 255.32
Lawson Number (LN): 16405; 8629; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
Atom/Bond Notes:
1. CIP Descriptor: Z

=> d pre

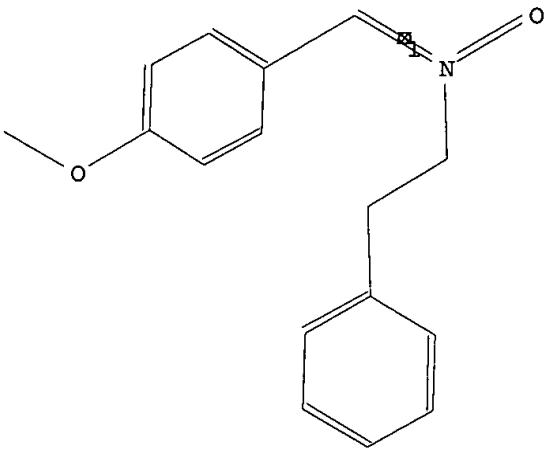
L13 ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Preparation:
PRE
Start: BRN=471382 4-methoxy-benzaldehyde, BRN=2079624
N-phenethyl-hydroxylamine
Time: 30 min
Solv: ethanol
Heating
ByProd: BRN=7077776 C16H17NO2
Reference(s):
1. Sivasubramanian, Shanmugaperumal; Mohan, Ponnusamy; Thirumalaikumar, Muniappan; Muthusubramanian, Shanmugan, J.Chem.Soc.Perkin Trans.1, <1994> 23, 3353-3354, LA: EN, CODEN: JCPRB4
Note(s):
2. Yield given. Yields of byproduct given

=> d ide 2

L13 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 7077776 Beilstein
Molecular Formula (MF): **C16 H17 N O2**
Beilstein Reference (SO): 6-15
General Comments (NTE): Stereo compound
Rltd. Stereoisomers (RSI): 7077777
Formula Weight (FW): 255.32
Lawson Number (LN): 16405; 8629; 289



Atom/Bond Notes:
1. CIP Descriptor: E

=> d pre 2

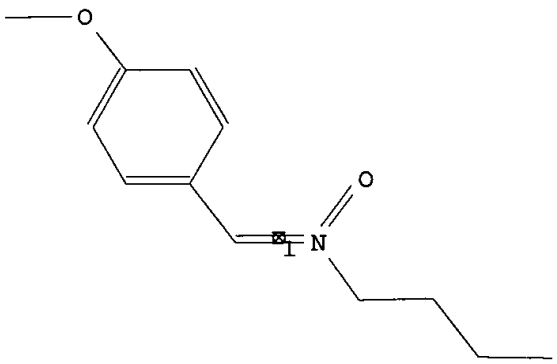
L13 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Preparation:
PRE
Start: BRN=471382 4-methoxy-benzaldehyde, BRN=2079624 N-phenethyl-hydroxylamine
Time: 30 min
Solv: ethanol
Heating
ByProd: BRN=7077777 C16H17NO2
Reference(s):
1. Sivasubramanian, Shanmugaperumal; Mohan, Ponnusamy; Thirumalaikumar, Muniappan; Muthusubramanian, Shanmugan, J.Chem.Soc.Perkin Trans.1, <1994> 23, 3353-3354, LA: EN, CODEN: JCPRB4
Note(s):
2. Yield given. Yields of byproduct given

=> d ide 3

L13 ANSWER 3 OF 3 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 6968329 Beilstein
Molecular Formula (MF): **C12 H17 N O2**
Beilstein Reference (SO): 6-08
General Comments (NTE): Stereo compound
Formula Weight (FW): 207.27
Lawson Number (LN): 8629; 3636; 289



Atom/Bond Notes:
1. CIP Descriptor: Z

=> d pre 3

L13 ANSWER 3 OF 3 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	54.52	353.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-6.43

FILE 'CAPLUS' ENTERED AT 17:07:36 ON 06 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1967 - 6 Jun 1999 VOL 130 ISS 24
FILE LAST UPDATED: 5 Jun 1999 (19990605/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s Chem?/so and Perkin?/so and Trans?/so and 23/so and 3353/so

1588765 CHEM?/SO
25213 PERKIN?/SO
233755 TRANS?/SO
334238 23/SO
10827 3353/SO

L14 1 CHEM?/SO AND PERKIN?/SO AND TRANS?/SO AND 23/SO AND 3353/SO

=> d ibib abs

L14 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:258379 CAPLUS
DOCUMENT NUMBER: 122:160227
TITLE: Synthesis and separation of the E and Z isomers of simple aldonitrones
AUTHOR(S): Sivasubramanian, Shanmugaperumal; Mohan, Ponnusamy; Thirumalaikumar, Muniappan; Muthusubramanian, Shanmugan
CORPORATE SOURCE: Dep. Org. Chem., Madurai Kamaraj Univ., Madurai, 625 021, India
SOURCE: J. **Chem**. Soc., **Perkin Trans**. 1 (1994), (**23**), **3353**-4
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:160227
AB The uncommon E isomer of simple aldonitrones has been obtained in significant amts. for the first time in the case of .alpha.-phenyl-N-(.beta.-phenylethyl)nitrones.

=> sel rn

E1 THROUGH E34 ASSIGNED

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.94	363.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.54	-6.97

FILE 'REGISTRY' ENTERED AT 17:09:18 ON 06 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

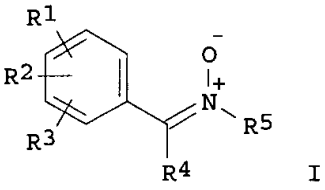
L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:282195 CAPLUS
DOCUMENT NUMBER: 130:311617
TITLE: Preparation of .alpha.-aryl-N-alkylnitrones for treatment of neurodegenerative, autoimmune, and inflammatory disease and as analytical reagents for detection of free radicals.
INVENTOR(S): Kelleher, Judith A.; Maples, Kirk R.; Dykman, Alina; Zhang, Yong-Kang; Wilcox, Allan L.; Levell, Julian
PATENT ASSIGNEE(S): Centaur Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920601	A1	19990429	WO 98-US21624	19981016

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 97-62324	19971017
	US 97-63736	19971029
	US 98-90475	19980624

OTHER SOURCE(S): MARPAT 130:311617
GI



I

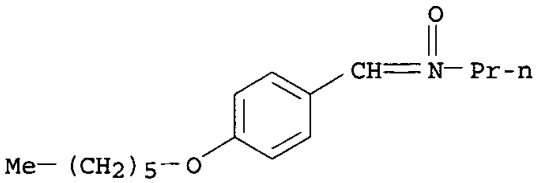
AB Title compds. [I; R1 = alkoxy, alkaryloxy, alkcycloalkoxy, aryloxy, cycloalkoxy; R2 = H, alkoxy, alkcycloalkoxy, cycloalkoxy, halo; adjacent R1R2 = alkylenedioxy; R3 = H, alkoxy, alkcycloalkoxy, cycloalkoxy, halo; R4 = H, alkyl; R5 = (substituted) alkyl, cycloalkyl; with provisos], were prepd. Thus, 4-hydroxybenzaldehyde was refluxed 30 min. with NaOH in EtOH; I(CH2)5CH3 was added and the mixt. was refluxed 68 h to give a residue which was kept 18 h with PrNO2, NH4Cl, and Zn in EtOH/H2O to give 12.4% .alpha.-4-hexyloxyphenyl-N-propylnitrone. Several I at 100 mg/kg orally in rats treated with M. tuberculin in incomplete Freunds adjuvant reduced CNS inflammatory deficit.

=> d hitstr

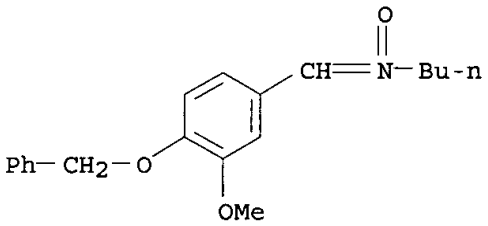
L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 1999 ACS
IT **223649-61-4P 223649-84-1P 223649-85-2P**
223649-86-3P 223649-87-4P 223650-08-6P

223650-16-6P 223650-17-7P 223650-39-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-aryl-N-alkylnitrones for treatment of neurodegenerative, autoimmune, and inflammatory disease and as anal. reagents for detection of free radicals)

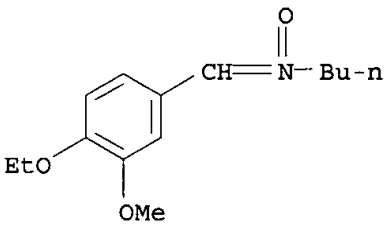
RN 223649-61-4 CAPLUS
CN 1-Propanamine, N-[[4-(hexyloxy)phenyl]methylene]-, N-oxide (9CI) (CA INDEX NAME)



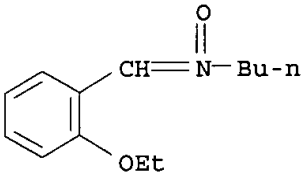
RN 223649-84-1 CAPLUS
CN 1-Butanamine, N-[[3-methoxy-4-(phenylmethoxy)phenyl]methylene]-, N-oxide (9CI) (CA INDEX NAME)



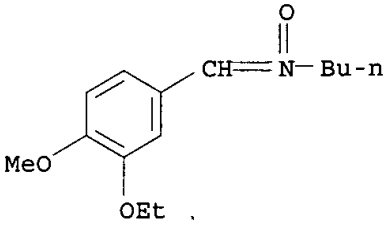
RN 223649-85-2 CAPLUS
CN 1-Butanamine, N-[(4-ethoxy-3-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



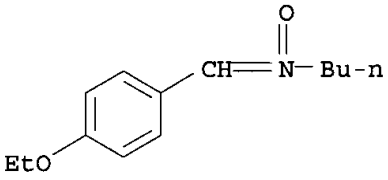
RN 223649-86-3 CAPLUS
CN 1-Butanamine, N-[(2-ethoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



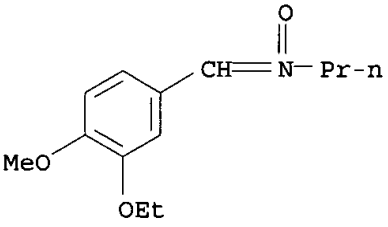
RN 223649-87-4 CAPLUS
CN 1-Butanamine, N-[(3-ethoxy-4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



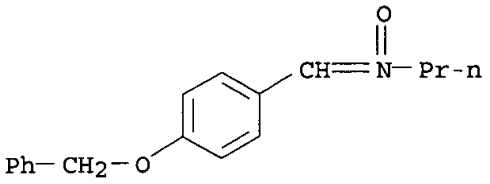
RN 223650-08-6 CAPLUS
CN 1-Butanamine, N-[(4-ethoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



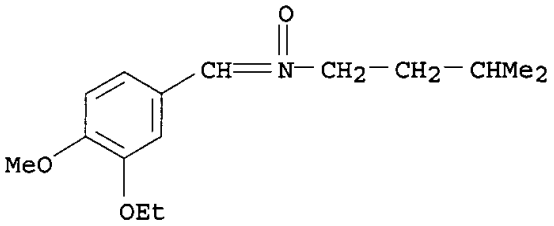
RN 223650-16-6 CAPLUS
CN 1-Propanamine, N-[(3-ethoxy-4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



RN 223650-17-7 CAPLUS
CN 1-Propanamine, N-[[4-(phenylmethoxy)phenyl]methylene]-, N-oxide (9CI) (CA INDEX NAME)



RN 223650-39-3 CAPLUS
CN 1-Butanamine, N-[(3-ethoxy-4-methoxyphenyl)methylene]-3-methyl-, N-oxide (9CI) (CA INDEX NAME)



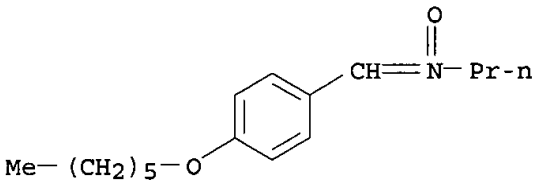
=> d ibib abs 2

L11 ANSWER 2 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:269363 CAPLUS
DOCUMENT NUMBER: 131:5082
TITLE: Unexpected reaction of .alpha.-aryl-N-(.beta.-phenylethyl) nitrones with chlorinating agents
AUTHOR(S): Mohan, Ponnusamy; Vanangamudi, Arumugasamy; Thirumalaikumar, Muniappan; Muthusubramanian, Shanmugam; Sivasubramanian, Shunmugaperumal
CORPORATE SOURCE: Department of Chemistry, The American College, Madurai, 625 002, India
SOURCE: Synth. Commun. (1999), 29(11), 2013-2017
CODEN: SYNCAV; ISSN: 0039-7911
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.-aryl-N-(.beta.-phenylethyl)nitrones when subjected to SO2Cl2/Et3N and NCS/NaOMe treatment independently, gave unexpectedly the corresponding amides. These procedures form an alternative route for the rearrangement of nitrones to amides.

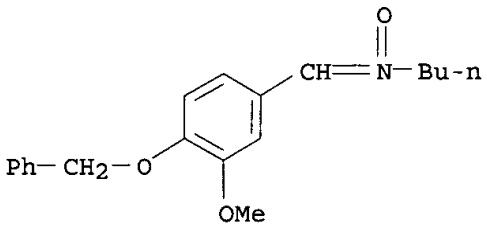
=> d hitstr

L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 1999 ACS
IT **223649-61-4P 223649-84-1P 223649-85-2P**
223649-86-3P 223649-87-4P 223650-08-6P
223650-16-6P 223650-17-7P 223650-39-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-aryl-N-alkylnitrones for treatment of neurodegenerative, autoimmune, and inflammatory disease and as anal. reagents for detection of free radicals)
RN 223649-61-4 CAPLUS

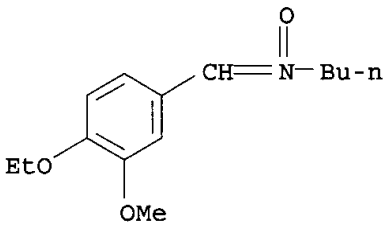
CN 1-Propanamine, N-[[4-(hexyloxy)phenyl]methylene]-, N-oxide (9CI) (CA INDEX NAME)



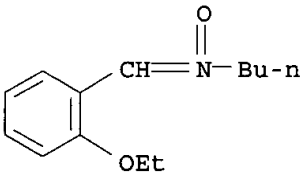
RN 223649-84-1 CAPLUS
CN 1-Butanamine, N-[[3-methoxy-4-(phenylmethoxy)phenyl]methylene]-, N-oxide (9CI) (CA INDEX NAME)



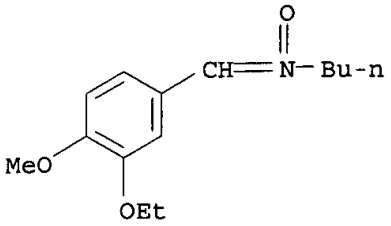
RN 223649-85-2 CAPLUS
CN 1-Butanamine, N-[(4-ethoxy-3-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



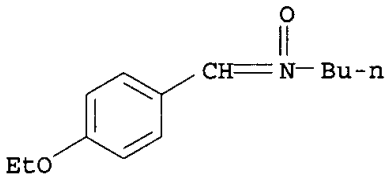
RN 223649-86-3 CAPLUS
CN 1-Butanamine, N-[(2-ethoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



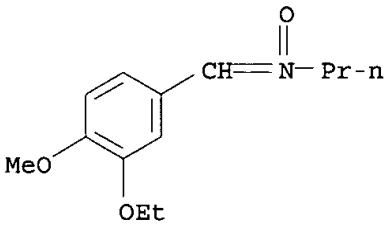
RN 223649-87-4 CAPLUS
CN 1-Butanamine, N-[(3-ethoxy-4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



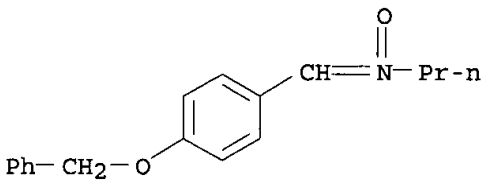
RN 223650-08-6 CAPLUS
CN 1-Butanamine, N-[(4-ethoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



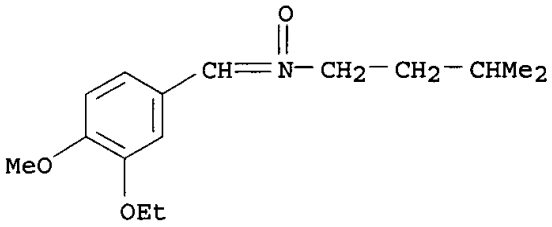
RN 223650-16-6 CAPLUS
CN 1-Propanamine, N-[(3-ethoxy-4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



RN 223650-17-7 CAPLUS
CN 1-Propanamine, N-[[4-(phenylmethoxy)phenyl]methylene]-, N-oxide (9CI) (CA INDEX NAME)



RN 223650-39-3 CAPLUS
CN 1-Butanamine, N-[(3-ethoxy-4-methoxyphenyl)methylene]-3-methyl-, N-oxide (9CI) (CA INDEX NAME)



=> d ibib abs hitstr 3

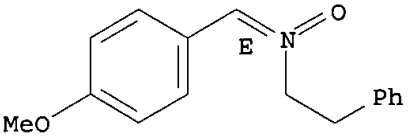
L11 ANSWER 3 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:258379 CAPLUS
DOCUMENT NUMBER: 122:160227
TITLE: Synthesis and separation of the E and Z isomers of simple aldonitrones
AUTHOR(S): Sivasubramanian, Shanmugaperumal; Mohan, Ponnusamy; Thirumalaikumar, Muniappan; Muthusubramanian, Shanmugan
CORPORATE SOURCE: Dep. Org. Chem., Madurai Kamaraj Univ., Madurai, 625 021, India
SOURCE: J. Chem. Soc., Perkin Trans. 1 (1994), (23), 3353-4
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:160227

AB The uncommon E isomer of simple aldonitrones has been obtained in significant amts. for the first time in the case of .alpha.-phenyl-N-(.beta.-phenylethyl)nitrones.

IT **161325-26-4P 161325-27-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sepn. of the E and Z isomers of simple aldonitrones and isomerization and)

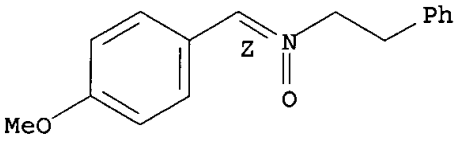
RN 161325-26-4 CAPLUS
CN Benzeneethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



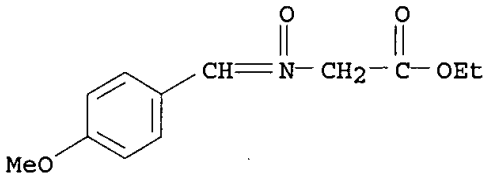
RN 161325-27-5 CAPLUS
CN Benzeneethanamine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



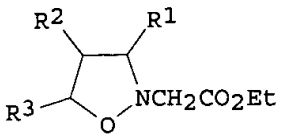
=> d ibib abs hitstr 4

L11 ANSWER 4 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:245708 CAPLUS
DOCUMENT NUMBER: 120:245708
TITLE: Synthesis of N-hydroxy-.alpha.-amino acid esters
AUTHOR(S): Seo, Min Hyo; Wang, Han Cheol; Lee, Youn Young; Goo, Yang Mo
CORPORATE SOURCE: Dep. Chem., Seoul Natl. Univ., Seoul, 151-742, S. Korea
SOURCE: J. Korean Chem. Soc. (1993), 37(9), 837-44
CODEN: JKCSEZ; ISSN: 1017-2548
DOCUMENT TYPE: Journal
LANGUAGE: Korean
OTHER SOURCE(S): CASREACT 120:245708
AB N-Arylmethylideneglycine N-oxide alkyl esters RCH:N(O)CH2CO2R1 (R = Ph, 4-MeOC6H4, 3-O2NC6H4; R1 = Et, CMe3, CH2Ph) were alkylated with alkyl halides R2Br or R2I (R2 = Me, PhgCH2, Me2CH, Et) in THF using LiN(SiMe3)2 as a base, followed by hydroxylaminolysis to give N-hydroxy-.alpha.-amino acid esters HONHCR2R3CO2R1 (R3 = H, Me, Et).
IT **154344-11-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(deprotonation and alkylation in prepn. of hydroxyamino acid esters)
RN 154344-11-3 CAPLUS
CN Glycine, N-[(4-methoxyphenyl)methylene]-, ethyl ester, N-oxide (9CI) (CA INDEX NAME)



=> d ibib abs 5 hitstr

L11 ANSWER 5 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:244787 CAPLUS
DOCUMENT NUMBER: 120:244787
TITLE: Preparation of N-carbethoxymethyl-C-alkyl(or aryl)nitrones and their 1,3-dipolar cycloaddition to alkenes
AUTHOR(S): Seo, Min Hyo; Wang, Han Cheol; Lee, Youn Young; Goo, Yang Mo; Kim, Kyongtae
CORPORATE SOURCE: Dep. Chem., Seoul Natl. Univ., Seoul, 151-742, S. Korea
SOURCE: Bull. Korean Chem. Soc. (1993), 14(5), 539-40
CODEN: BKCSDE; ISSN: 0253-2964
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:244787
GI



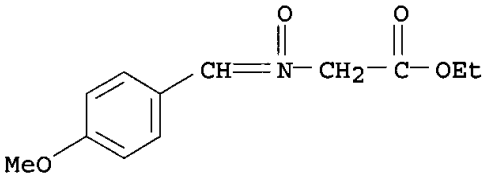
I

AB Reaction of HONHCH2CO2Et with RCHO (R = Me, Et, Pr, Me2CH, HOCH2CMe2, 2-HOC6H4, 4-HOC6H4, 4-MeOC6H4, 4-ClC6H4, 4-O2NC6H4, 3-O2NC6H4, 4-Me2NC6H4) in C6H6 gave 85-100% title nitrones, CHR:N+O-CH2CO2Et, which on cycloaddn. with alkenes in C6H6 gave 10-96% isoxazolidines I (R1 = Et, Pr, R2 = R3 = CO2Et; R1 = Pr, R2 = H, R3 = CO2Me; R1 = Pr, R2 = CO2Et, R3 = Me; R1 = 4-O2NC6H4, R2 = H, R3 = CO2Me; R1 = 4-O2NC6H4, R2 = CO2Me, R3 = H).

IT **154344-11-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 154344-11-3 CAPLUS

CN Glycine, N-[(4-methoxyphenyl)methylene]-, ethyl ester, N-oxide (9CI) (CA INDEX NAME)



=> d ibib abs 6-7 hitstr

L11 ANSWER 6 OF 13 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1990:158107 CAPLUS

DOCUMENT NUMBER: 112:158107

TITLE: Studies on intramolecular 1,3-dipolar cycloaddition reactions. III. The synthesis of a novel heterocyclic ring system by regiospecific cycloaddition

AUTHOR(S): Chen, Qinghua; Yu, Xiuzhi; Zhang, Tieyuan; Jia, Xibei

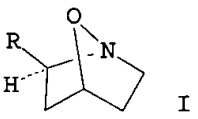
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China

SOURCE: Acta Chim. Sin. (Engl. Ed.) (1989), (2), 176-82
CODEN: ACSIEW

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

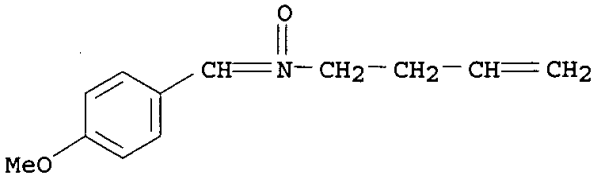
AB RCH:N(O)CH2CH2CH:CH2 [I; R = (un)substituted phenyl, 2-furyl, 2-thienyl,

pyrrol-2-yl] were prepd. in 43-70% yield by reaction of (Z)-RCH:NOH with BrCH2CH2CH:CH2 in EtONa/EtOH.

IT **126088-30-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and intramol. cycloaddn. reaction of)

RN 126088-30-0 CAPLUS

CN 3-Buten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)- (9CI) (CA INDEX NAME)



L11 ANSWER 7 OF 13 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1989:533451 CAPLUS

DOCUMENT NUMBER: 111:133451

TITLE: Intramolecular 1,3-dipolar cycloaddition reactions. IV. Thermochemical and photochemical reactions of some 1,3-dipolar nitrone systems and their regioselectivities

AUTHOR(S): Chen, Qinghua; Xie, Mengxia; Jia, Xibei; Wang, Xueliang

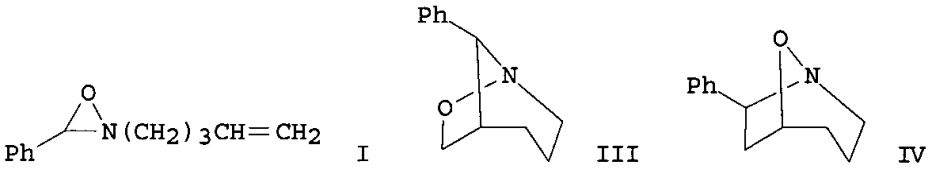
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China

SOURCE: Youji Huaxue (1989), 9(2), 156-62
CODEN: YCHHDX; ISSN: 0253-2786

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI

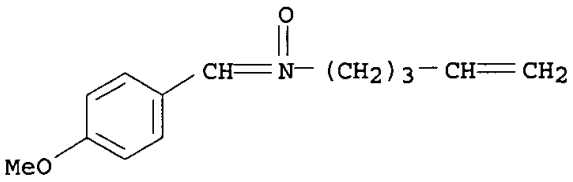


AB The substituent effects on the reactivities and the regioselectivities of the title reactions were examd. by chromatog. methods. On irradn. by a Hg lamp at .lambda. .gtoreq.302 nm, nitrones, e.g., CHPh:N(O)(CH2)3CH:CH2, gave oxaziridine I. I rearranged further to BzNH(CH2)3CH:CH2 (II) at .lambda. .gtoreq.270 nm. Upon heating, II was transformed back to the nitrone and subsequently cyclized to give III and IV.

IT **122753-93-9**
RL: RCT (Reactant)
(photolysis of)

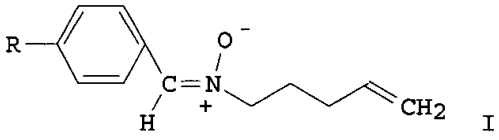
RN 122753-93-9 CAPLUS

CN 4-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)

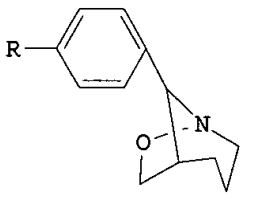


=> d ibib abs hitstr 8-10

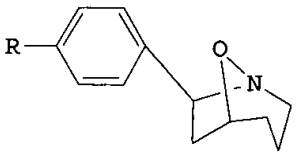
L11 ANSWER 8 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1987:515572 CAPLUS
DOCUMENT NUMBER: 107:115572
TITLE: Intramolecular 1,3-dipolar cycloaddition reactions. I. Thermochemical reactivities and regioselectivities of 4-substituted phenyl(N-4-pentenyl)nitrones
AUTHOR(S): Chen, Qinghua; Meng, Min
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China
SOURCE: Huaxue Xuebao (1986), 44(9), 927-33
CODEN: HHHPA4; ISSN: 0567-7351
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 107:115572
GI



I



VI



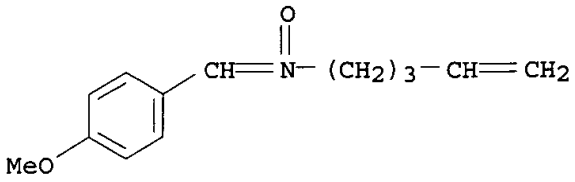
VII

AB Refluxing nitrones I [R = NO2 (II), Br (III), H (IV), MeO (V)] in toluene for 24 h gave 54-80% cycloadducts VI and VII (VI/VII = 2). The thermochem. reactivity is in the order of II > III > IV > V.

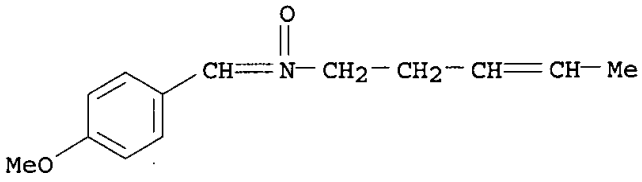
IT **109830-20-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cycloaddn. reaction of)

RN 109830-20-8 CAPLUS

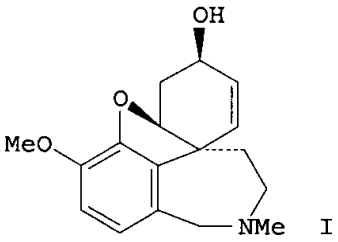
CN 4-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z)- (9CI) (CA INDEX NAME)



IT **109830-28-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 109830-28-6 CAPLUS
CN 3-Penten-1-amine, N-[(4-methoxyphenyl)methylene]-, N-oxide, (Z,E)- (9CI)
(CA INDEX NAME)



L11 ANSWER 9 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1986:403203 CAPLUS
DOCUMENT NUMBER: 105:3203
TITLE: Microbial transformations of galanthamine precursors
AUTHOR(S): Spassov, G.; Abraham, W. R.; Kieslich, K.; Vlahov, R.; Krikozian, D.; Parushev, S.; Chinova, M.; Snatzke, G.
CORPORATE SOURCE: Inst. Org. Chem., Sofia, 1113, Bulg.
SOURCE: Appl. Microbiol. Biotechnol. (1986), 23(3-4), 206-10
CODEN: AMBIDG; ISSN: 0175-7598
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



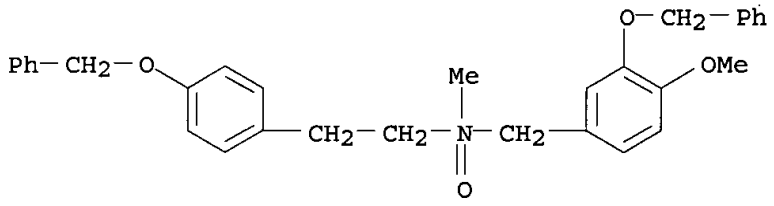
AB Galanthamine (I), a medically important alkaloid, gives a racemic product in low yields when prepd. by chem. synthesis. Starting with a belladine deriv. an enzymic ring closure should lead exclusively to a chiral product possibly with the native structure. Although this reaction type is unknown in preparative biotransformations a large no. of microorganisms were tested, but without success. On the other hand, transformation products were found resulting from specific dealkylations of the substrate. The type of metabolite formed was dependent on the fungi

utilized for the transformation. Addnl., 2 N-oxides were formed by Septomyxa affins, one in good yield. It is possible that the chirality of this compd. can direct the ring closure preferentially or exclusively to the desired stereoisomer of narwedine.

IT **102743-22-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, fermentative)

RN 102743-22-6 CAPLUS

CN Benzeneethanamine, N-[[4-methoxy-3-(phenylmethoxy)phenyl]methyl]-N-methyl-4-(phenylmethoxy)-, N-oxide (9CI) (CA INDEX NAME)



L11 ANSWER 10 OF 13 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1985:5798 CAPLUS

DOCUMENT NUMBER: 102:5798

TITLE: Ring-chain isomerism of N-(1-carboxyalkyl)nitrones. I. C-Aryl-N-(1-carboxylalkyl)nitrones

AUTHOR(S): Kliegel, Wolfgang; Graumann, Juergen

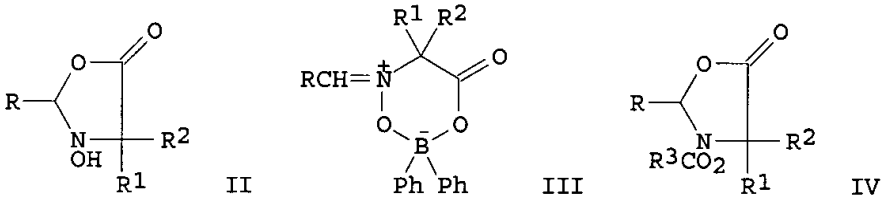
CORPORATE SOURCE: Inst. Pharm. Chem., Tech. Univ. Braunschweig, Braunschweig, D-3300, Fed. Rep. Ger.

SOURCE: Liebigs Ann. Chem. (1984), (9), 1545-62
CODEN: LACHDL; ISSN: 0170-2041

DOCUMENT TYPE: Journal

LANGUAGE: German

GI

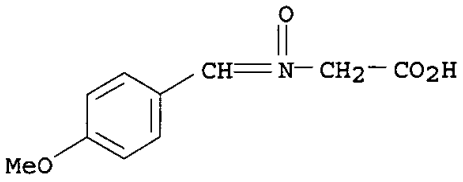


AB RCH:N+(O-)CR1R2CO2H [I; R = (un)substituted Ph; R1 = H, Me, Ph; R2 = H, Me, Et; R1R2 = (CH2)4, (CH2)5] were prepd. by alkylation of (Z)-RCH:NOH with R1R2CBrCO2H or by condensation of HONHCR1R2CO2H with RCHO. The ring-chain isomerism between nitrone I and oxazolidine II could not be proven spectroscopically. Acylating I with (Ph2B)2O gave boron chelates III of the open-chain nitrone form, while acylating with carboxylic acids or isocyanates gave oxazolidones IV [R3 = Me, 3,5-(O2N)2C6H3, 3-ClC6H4NH]. Alkylating I with PhCOCH2Br gave esters RCH:N+(O-)CR1R2CO2CH2COPh.

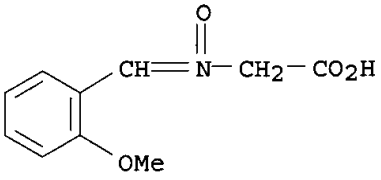
IT **17556-16-0P 93562-95-9P 93563-06-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of, with oxybis(diphenylborane))

RN 17556-16-0 CAPLUS

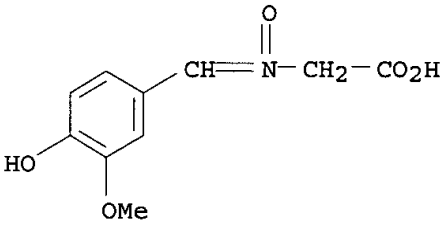
CN Glycine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



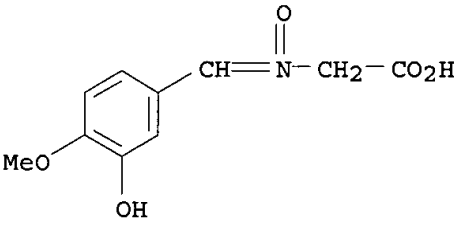
RN 93562-95-9 CAPLUS
CN Glycine, N-[(2-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



RN 93563-06-5 CAPLUS
CN Glycine, N-[(4-hydroxy-3-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



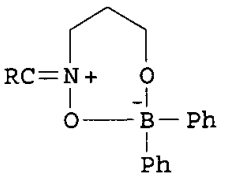
IT **93563-07-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 93563-07-6 CAPLUS
CN Glycine, N-[(3-hydroxy-4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



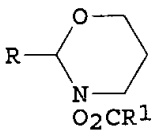
=> d ibib abs hitstr 11-13

L11 ANSWER 11 OF 13 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1984:138667 CAPLUS
DOCUMENT NUMBER: 100:138667
TITLE: Ring-chain isomerism of N-(3-hydroxyalkyl)nitrones. I. C-Aryl-N-(3-hydroxypropyl)nitrones
AUTHOR(S): Kliegel, Wolfgang; Preu, Lutz
CORPORATE SOURCE: Inst. Pharm. Chem., Tech. Univ. Braunschweig, Braunschweig, D-3300, Fed. Rep. Ger.
SOURCE: Liebigs Ann. Chem. (1983), (11), 1937-49
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



II

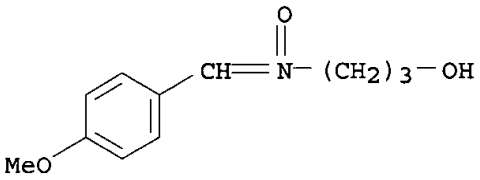


III

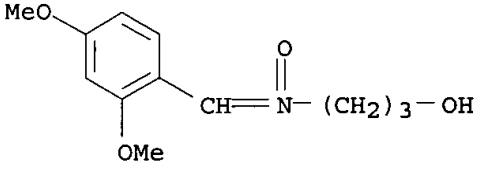
AB RHC:N+(O-)(CH2)3OH [I, R = Ph, p-O2NC6H4, 4-ClC6H4, 4-MeOC6H4, 2,4-(MeO)2C6H3, p-Me2NC6H4, 3,4-MeO(HO)C6H3] were prepd. by oxidn. of PhCH:N(CH2)3OH with AcOOH followed by hydrolysis and condensation of the 3-(hydroxyamino)propanol with RCHO. The isomerization of I and perhydro-1,3-oxazines was shown by the formation of diphenylboron chelates II and acyloxyperhydrooxazines III (R1 = Ph, p-O2NC6H4).

IT **88690-68-0P 88690-69-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ring-chain isomerization of)

RN 88690-68-0 CAPLUS
CN 1-Propanol, 3-[[(4-methoxyphenyl)methylene]oxidoamino]- (9CI) (CA INDEX NAME)

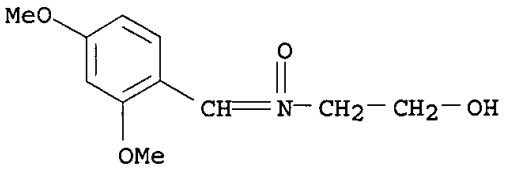


RN 88690-69-1 CAPLUS
CN 1-Propanol, 3-[[(2,4-dimethoxyphenyl)methylene]oxidoamino]- (9CI) (CA INDEX NAME)

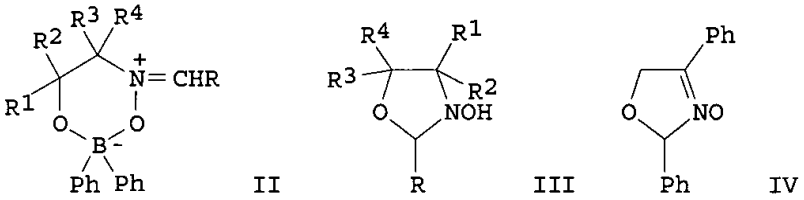


IT **88690-85-1P**

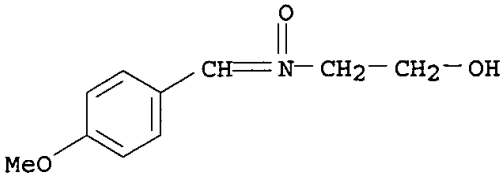
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 88690-85-1 CAPLUS
CN Ethanol, 2-[[(2,4-dimethoxyphenyl)methylene]oxidoamino]- (9CI) (CA INDEX NAME)



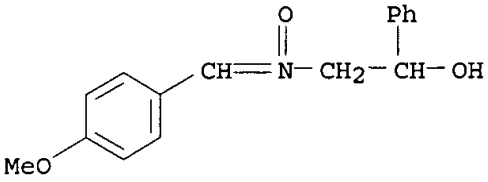
L11 ANSWER 12 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1977:502398 CAPLUS
DOCUMENT NUMBER: 87:102398
TITLE: Ring-chain isomerism of N-(2-hydroxyalkyl)nitrones. I. Nitrones of substituted benzaldehydes
AUTHOR(S): Kliegel, Wolfgang; Becker, Harald
CORPORATE SOURCE: Inst. Pharm. Chem., Tech. Univ. Braunschweig, Braunschweig, Ger.
SOURCE: Chem. Ber. (1977), 110(6), 2067-89
CODEN: CHBEAM
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



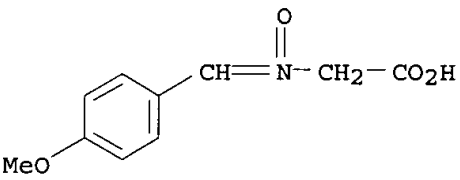
AB Condensation of HONHCR1R2CR3R4OH with RCHO gave 30-100% 41 HOCR3R4CR1R2N+(O-):CHR [I, R = Ph, p-tolyl, p-anisyl, 2,6-Cl2C6H3, o-, m-, p-O2NC6H4, p-Me2NC6H4; etc; R1, R3 = H, Me, Et, Ph; R2 = H, Me; R4 = H; R3R4 = (CH2)5]. Cyclization of I with Ph2BX (X = OBPh2, Ph) gave 23-100% 41 1,3-dioxa-4-azonia-2-boratacyclohexanes II. The hydoxyl groups of I and its isomer III were acylated to give .apprx.10 esters and III (R = R1 = Ph, R2-R4 = H) was oxidized to give IV.
IT **63829-49-2P 63829-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with boron compds.)
RN 63829-49-2 CAPLUS
CN Ethanol, 2-[[(4-methoxyphenyl)methylene]oxidoamino]- (9CI) (CA INDEX NAME)



RN 63829-54-9 CAPLUS
CN Benzenemethanol, .alpha.-[[[(4-methoxyphenyl)methylene]oxidoamino]methyl]-
(9CI) (CA INDEX NAME)



L11 ANSWER 13 OF 13 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1969:11283 CAPLUS
DOCUMENT NUMBER: 70:11283
TITLE: Improved synthesis of anti-benzaldoxime. Concomitant cleavage and formylation of nitrones
AUTHOR(S): Schoenewaldt, Erwin F.; Kinnel, Robin B.; Davis Paul
CORPORATE SOURCE: Res. Lab. Div., Merck and Co., Inc., Rahway, N. J., USA
SOURCE: J. Org. Chem. (1968), 33(11), 4270-2
CODEN: JOCEAH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB BzH is oximated, syn-benzaldoxime, (syn-I) sepd. by C6H6 extn., and the C6H6 soln. refluxed and treated with HCl to give anti-I.HCl which is converted to anti-I; anti-anisaldoxime is prepd. similarly. The anti-benzaldoximes are converted to N-(carboxymethyl)-.alpha.-[p-(R-substituted)-phenyl]nitrones (II).
IT **17556-16-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 17556-16-0 CAPLUS
CN Glycine, N-[(4-methoxyphenyl)methylene]-, N-oxide (9CI) (CA INDEX NAME)



=> file stnguide

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=> file beilstein

COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     0.00      -6.96

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FILE COVERS 1779 TO 1999.
*** CAS REGISTRY NUMBERS FOR 4,356,237 SUBSTANCES AVAILABLE ***
*** FILE CONTAINS 7,446,355 SUBSTANCES ***

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=>
Uploading 9172763.str

L12     STRUCTURE UPLOADED

=> d his


     (FILE 'HOME' ENTERED AT 18:16:34 ON 28 JUN 1999)

     FILE 'REGISTRY' ENTERED AT 18:16:38 ON 28 JUN 1999
L1              STRUCTURE UPLOADED
L2            2 S L1
L3           54 S L1 FULL
L4         1059 S NITRONE
L5            1 S L4 AND DIOXY?
L6            1 S L4 AND METHYLENEDIOXY?

     FILE 'STNGUIDE' ENTERED AT 18:22:56 ON 28 JUN 1999

     FILE 'REGISTRY' ENTERED AT 18:23:53 ON 28 JUN 1999
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L7            43 S L3 AND 1/N
L8            39 S L7 NOT PHENOL
L9            38 S L8 NOT S/ELS
L10           28 S L9 NOT B/ELS

     FILE 'CAPLUS' ENTERED AT 18:26:54 ON 28 JUN 1999
L11           13 S L10

     FILE 'STNGUIDE' ENTERED AT 18:30:01 ON 28 JUN 1999

     FILE 'BEILSTEIN' ENTERED AT 18:34:32 ON 28 JUN 1999
L12              STRUCTURE UPLOADED

=> d l12

L12 HAS NO ANSWERS
L12              STR
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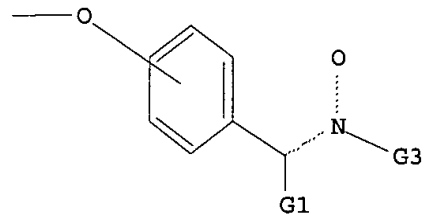

G1 H,Me,Et,n-Pr,n-Bu

G2 MeO,EtO,n-PrO,n-BuO,t-BuO,PhO

G3 Me,Et,n-Pr,n-Bu,s-Bu,t-Bu,Cb,Ak

Structure attributes must be viewed using STN Express query preparation.

```
=> s l12 full

FULL SEARCH INITIATED 18:35:06 FILE 'BEILSTEIN'
SCREENING
FULL SCREEN SEARCH COMPLETED -  56340 TO ITERATE
 17.5% PROCESSED    9850 ITERATIONS                              49 ANSWERS
<------User Break------>
u
 61.1% PROCESSED   34425 ITERATIONS                             148 ANSWERS
SEARCH ENDED BY USER
SEARCH TIME: 00.01.07

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        56340 TO    56340
PROJECTED ANSWERS:             196 TO      288

L13         148 SEA SSS FUL L12

=> d die

'DIE' IS NOT A VALID FORMAT FOR FILE 'BEILSTEIN'

The following are valid formats:

QRD --------- Query Related Data (IDE plus HIT)
IDE --------- Identification of Substance, plus Structure
  (BRN, MF, LSF, CN, SY, AUN, FW, SO, NTE, LN, RN, BPR, RSI, OS, STR)
GEN --------- General Data
```

```
ALL --------- All Display fields (Lengthy display!)
CHE --------- Chemical Data
PHY --------- Physical Data
HIT --------- All fields containing hit terms
Hit terms will be highlighted in all IDE fields in the BEILSTEIN file
A maximum of 20 values are displayed in each single property field.
Use DISPLAY F<prop> for FULL format, e.g. FBP instead of BP.
For more information about display formats, and how to display
individual selected properties, enter 'HELP FORMAT' at an arrow
prompt, e.g. => HELP FORMAT.
ENTER DISPLAY FORMAT (QRD):end


=> d ide


L13  ANSWER 1 OF 148  BEILSTEIN  COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN):    8029140  Beilstein
Molecular Formula (MF):      C42 H55 N3 O7
Autonom Name (AUN):          (2-<bis-(3-methoxy-benzyl)-amino>-ethyl)-(3-<N,N-
                             bis-(3-methoxy-benzyl)-aminooxy>-propyl)-carbamic
                             acid tert-butyl ester
Beilstein Reference (SO):    6-15
Formula Weight (FW):         713.91
Lawson Number (LN):          16413; 14901; 3131; 3018; 1762; 318; 289
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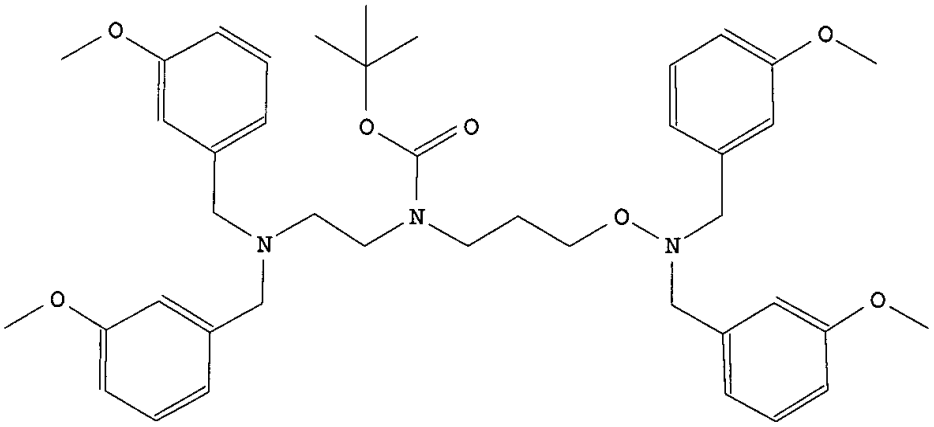

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Uploading 9172763.str

L12      STRUCTURE UPLOADE

=> d

L14 HAS NO ANSWERS
L14              STR
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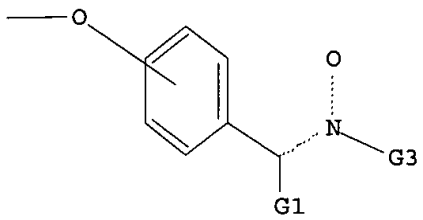


G1 H,Me,Et,n-Pr,n-Bu

G2 MeO,EtO,n-PrO,n-BuO,t-BuO,PhO

G3 Me,Et,n-Pr,n-Bu,s-Bu,t-Bu

Structure attributes must be viewed using STN Express query preparation.

=> s l14

SAMPLE SEARCH INITIATED 18:37:58 FILE 'BEILSTEIN'
SAMPLE SCREEN SEARCH COMPLETED - 503 TO ITERATE
100.0% PROCESSED 503 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.07

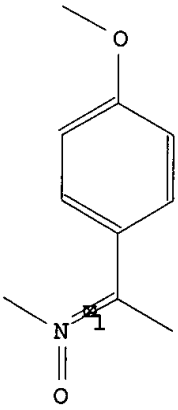
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8716 TO 11404
PROJECTED ANSWERS: 5 TO 234

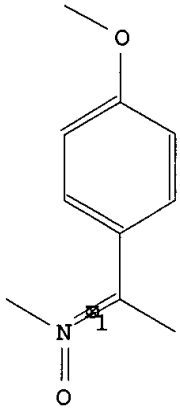
L15 5 SEA SSS SAM L14

=> d ide

L15 ANSWER 1 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 6800927 Beilstein
Molecular Formula (MF): C10 H13 N O2
Beilstein Reference (SO): 6-08
General Comments (NTE): Stereo compound; Referenced by other compounds
Formula Weight (FW): 179.22
Lawson Number (LN): 8639; 3625; 289





Atom/Bond Notes:
1. CIP Descriptor: E

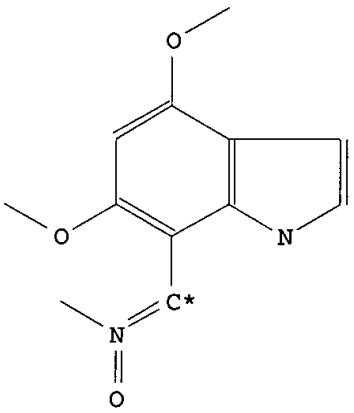
=> d pre

L15 ANSWER 1 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

=> d ide 2

L15 ANSWER 2 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN):	6144950 Beilstein
Molecular Formula (MF):	C12 H14 N2 O3
Synonym (SY):	N-(4',6'-dimethoxyindol-7'-ylmethylene)methylamine N-oxide
Beilstein Reference (SO):	6-21
Formula Weight (FW):	234.25
Lawson Number (LN):	26138; 3625; 289



=> d pre 2

L15 ANSWER 2 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Preparation:
PRE
Start: BRN=6149124 4,6-dimethoxy-1-(3'-methyl-1'-oxobut-2'-enyl)indole-7-carbaldehyde, BRN=3541409 N-methyl-hydroxylamine; hydrochloride
Reag: aq. AcONa
Time: 12 hour(s)
Yield: 42.00 %
Solv: ethanol
Heating
Reference(s):
1. Black, David St. C.; Keller, Paul A.; Kumar, Naresh, Aust.J.Chem., 46 <1993> 6, 843-862, LA: EN, CODEN: AJCHAS

=> d ide 3

L15 ANSWER 3 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 4923229 Beilstein
Molecular Formula (MF): 2 C9 H11 N O2 . H I
Chemical Name (CN): 4-methoxy-benzaldehyde-<N-methyl oxime >; hydriodide
4-Methoxy-benzaldehyd-<N-methyl-oxim>; Hydrojodid
Beilstein Reference (SO): 2-08-00-00068

Component Data:

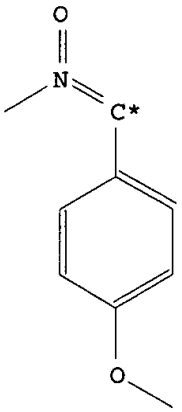
Component Reg. No. (CBRN)	Component Molec. Formula (CMF)	Formula Weight (FW)	Lawson Number (LN)
4750	C9 H11 N O2	165.19	8629, 3625, 289
3587159	H I	127.91	

CM 1

CBRN 3587159
CMF H I

CM 2

CBRN 4750
CMF C9 H11 N O2



=> d pre

L15 ANSWER 1 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

=> d pre 3

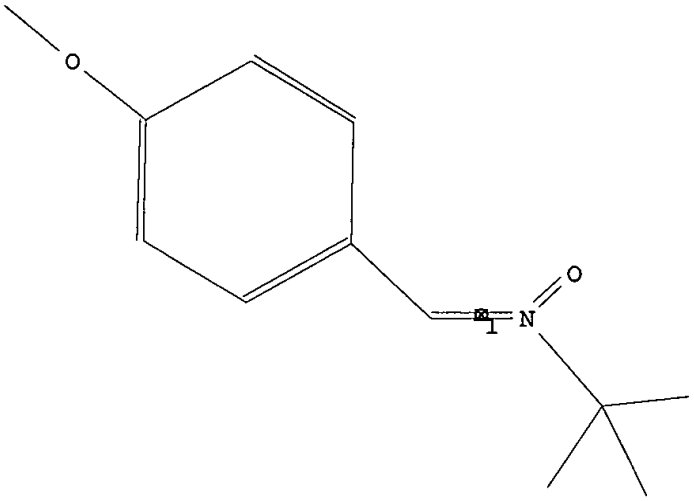
L15 ANSWER 3 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Preparation:
PRE
Start: .alpha.-anisaldoxime , methyl iodide
Detail: im Dunkeln
Reference(s):
1. Brady; Dunn; Goldstein, J.Chem.Soc., 1926,2395, CODEN: JCSOA9
Note(s):
2. Handbook Data

=> d ide 4

L15 ANSWER 4 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN):	3542408 Beilstein
Molecular Formula (MF):	C12 H17 N O2
Synonym (SY):	4-methoxybenzylidene-t-butylamine-N-oxide
Beilstein Reference (SO):	6-08
General Comments (NTE):	Stereo compound
CAS Reg. No. (RN):	40117-28-0; 127896-00-8
Beilstein Pref. RN (BPR):	40117-28-0
Rltd. Stereoisomers (RSI):	2097499; 7424059
Formula Weight (FW):	207.27
Lawson Number (LN):	8629; 3638; 289



Atom/Bond Notes:
1. CIP Descriptor: Z

=> d pre 4

L15 ANSWER 4 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Preparation:
PRE
Start: BRN=3540128 tert-butyl-(4-methoxy-benzylidene)-amine
Reag: MCPBA
Solv: CDCl3
Temp: 0.0 Cel
Reference(s):
1. Boyd, Derek R.; Coulter, Peter B.; McGuckin, M. Rosaleen; Sharma, Narain D.; Jennings, W. Brian; Wilson, Valerie E., J.Chem.Soc.Perkin Trans.1, <1990> 2, 301-306, LA: EN, CODEN: JCPRB4
Note(s):
2. Yield given
PRE
Start: BRN=3540128 C12H17NO
Reag: MCPBA
Solv: CDCl3
Temp: 0.0 Cel
ByProd: BRN=1211550 C12H17NO2 \75 percent Spectr.
Reference(s):
1. Boyd, Derek R.; Coulter, Peter B.; Sharma, Narain D.; Jennings, Brian W.; Wilson, Valerie E., Tetrahedron Lett., 26 <1985> 13, 1673-1676, LA: EN, CODEN: TELEAY
Note(s):
2. Yield: 25 percent Spectr.
PRE
Start: BRN=471382 4-methoxy-benzaldehyde, BRN=1744184 2-methyl-2-nitro-propane
Reag: zinc, glacial acetic acid
Yield: 79.00 %
Solv: aq. ethanol
Detail: 1.) 10 deg C, 2 h, 2.) 6 deg C, 48 h
Reference(s):
1. Huie, Reeves; Cherry, William R., J.Org.Chem., 50 <1985> 9, 1531-1532, LA: EN, CODEN: JOCEAH

PRE
Start: BRN=1744184 2-methyl-2-nitro-propane, BRN=471382
4-methoxy-benzaldehyde
Reag: zinc/acetic aicd
Time: 2 hour(s)
Yield: 52.00 %
Solv: aq. ethanol
Ambient Temperature
Reference(s):
1. Hinton, Randall D.; Janzen, Edward, G., J.Org.Chem., 57 <1992> 9, 2646-2651, LA: EN, CODEN: JOCEAH

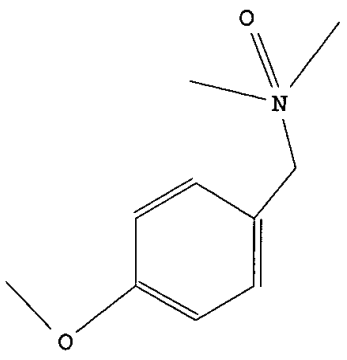
PRE
Start: BRN=1731503 N-tert-butyl-hydroxylamine, BRN=471382
4-methoxy-benzaldehyde
Time: 18 hour(s)
Yield: 13.20 %
Solv: benzene
Heating
Reference(s):
1. Bacon, W. E.; Neubert, M. E.; Wildman, P. J.; Ott, D. W., Mol.Cryst.Liq.Cryst., 90 <1983>, 307-322, LA: EN, CODEN: MCLCA5

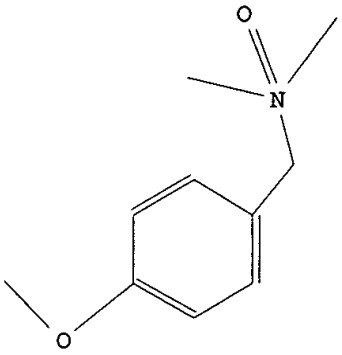
PRE
Start: BRN=1731503 N-tert-butyl-hydroxylamine, BRN=471382
4-methoxy-benzaldehyde
Reag: MgSO4
Time: 1 hour(s)
Yield: 63.00 %
Solv: 1,2-dichloro-ethane
Heating
Reference(s):
1. Chan, Kin Shing; Yeung, Ming Lok; Chan, Wai-kin; Wang, Ru-Ji; Mak, Thomas C. W., J.Org.Chem., 60 <1995> 6, 1741-1747, LA: EN, CODEN: JOCEAH

=> d ide 5

L15 ANSWER 5 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 2832568 Beilstein
Molecular Formula (MF): C10 H15 N O2
Synonym (SY): p-Methoxy-N,N-dimethylbenzylamin-N-oxid
Beilstein Reference (SO): 5-13
CAS Reg. No. (RN): 33930-46-0
Beilstein Pref. RN (BPR): 33930-46-0
Formula Weight (FW): 181.23
Lawson Number (LN): 14901; 2817; 289





=> d pre

L15 ANSWER 1 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

=> d pre 5

L15 ANSWER 5 OF 5 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Preparation:
PRE
Reference(s):
1. Bather et al., J.Chem.Soc.C, <1971>, 3060,3067, CODEN: JSOOAX

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	90.00	291.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-6.96

FILE 'CAPLUS' ENTERED AT 18:48:02 ON 28 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1967 - 28 Jun 1999 VOL 131 ISS 1
FILE LAST UPDATED: 28 Jun 1999 (19990628/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

```
=> d his


     (FILE 'HOME' ENTERED AT 18:16:34 ON 28 JUN 1999)

     FILE 'REGISTRY' ENTERED AT 18:16:38 ON 28 JUN 1999
L1              STRUCTURE UPLOADED
L2            2 S L1
L3           54 S L1 FULL
L4         1059 S NITRONE
L5            1 S L4 AND DIOXY?
L6            1 S L4 AND METHYLENEDIOXY?

     FILE 'STNGUIDE' ENTERED AT 18:22:56 ON 28 JUN 1999

     FILE 'REGISTRY' ENTERED AT 18:23:53 ON 28 JUN 1999
L7           43 S L3 AND 1/N
L8           39 S L7 NOT PHENOL
L9           38 S L8 NOT S/ELS
L10          28 S L9 NOT B/ELS

     FILE 'CAPLUS' ENTERED AT 18:26:54 ON 28 JUN 1999
L11          13 S L10

     FILE 'STNGUIDE' ENTERED AT 18:30:01 ON 28 JUN 1999

     FILE 'BEILSTEIN' ENTERED AT 18:34:32 ON 28 JUN 1999
L12             STRUCTURE UPLOADED
L13         148 S L12 FULL
L14             STRUCTURE UPLOADED
L15           5 S L14

     FILE 'CAPLUS' ENTERED AT 18:48:02 ON 28 JUN 1999

=> file reg

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.32     291.64

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -6.96

FILE 'REGISTRY' ENTERED AT 18:48:24 ON 28 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:   26 JUN  99  HIGHEST RN 226425-06-5
DICTIONARY FILE UPDATES:  27 JUN  99  HIGHEST RN 226425-06-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=> s  methylenedioxy?

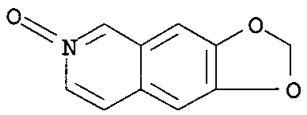
L16        9384 METHYLENEDIOXY?

=> s l16 and N-oxide
```

```
       2975109 N
        458795 OXIDE
           115 OXIDES
        458795 OXIDE
                  (OXIDE OR OXIDES)
         19024 N-OXIDE
                  (N(W)OXIDE)
L17          5 L16 AND N-OXIDE

=> d scan

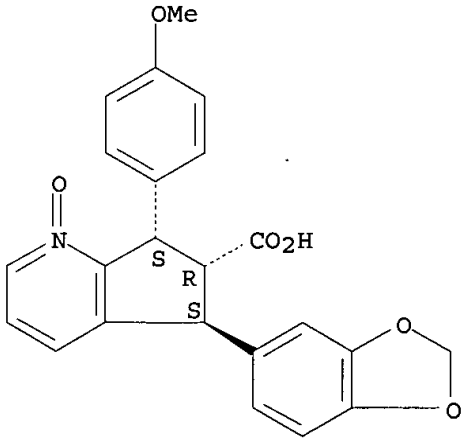

L17  5 ANSWERS   REGISTRY  COPYRIGHT 1999 ACS
IN   1,3-Dioxolo[4,5-g]isoquinoline, 6-oxide (9CI)
MF   C10 H7 N O3
```



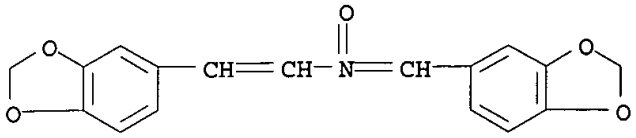
```
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5


L17  5 ANSWERS   REGISTRY  COPYRIGHT 1999 ACS
IN   5H-Cyclopenta[b]pyridine-6-carboxylic acid, 5-(1,3-benzodioxol-5-yl)-6,7-
     dihydro-7-(4-methoxyphenyl)-, 1-oxide, (5.alpha.,6.beta.,7.beta.)- (9CI)
MF   C23 H19 N O6

Relative stereochemistry.
```

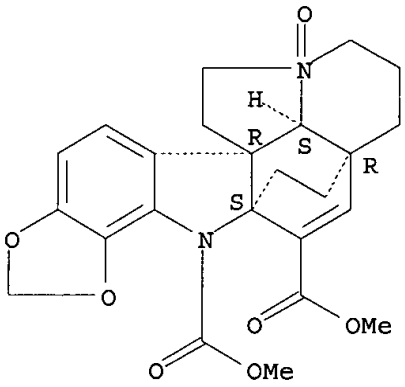


```
L17  5 ANSWERS   REGISTRY  COPYRIGHT 1999 ACS
IN   Styrylamine, 3,4-(methylenedioxy)-N-piperonylidene-, N-oxide (7CI)
MF   C17 H13 N O5
```

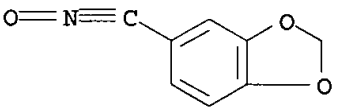


L17 5 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN 6H,14aH-3a,5a-Ethano-1H-[1,3]dioxolo[4,5-a]indolizino[1,8-fg]carbazole-5,6-dicarboxylic acid, 2,3,12,13-tetrahydro-, dimethyl ester, 14-oxide, (3aR,5aS,11bR,14aS)-[partial]- (9CI)
MF C24 H26 N2 O7

Absolute stereochemistry.



L17 5 ANSWERS REGISTRY COPYRIGHT 1999 ACS
IN **1,3-Benzodioxole-5-carbonitrile, N-oxide (9CI)**
MF C8 H5 N O3



ALL ANSWERS HAVE BEEN SCANNED

=>

=>
Executing the logoff script...

=> LOG H

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	11.55	303.19

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY     SESSION
CA SUBSCRIBER PRICE                                   0.00       -6.96

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 18:50:02 ON 28 JUN 1999
Trying 9351006...Open

Welcome to STN International!  Enter x:x
LOGINID:ssspta1204jxv
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2
```

=> s 131:85/dn

L1 1 131:85/DN

=> d ibib abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:338773 CAPLUS
DOCUMENT NUMBER: **131:85**
TITLE: Treating and preventing levodopa-induced dyskinesias: current and future strategies
AUTHOR(S): Durif, Franck
CORPORATE SOURCE: Federation de Neurologie, CHRU Clermont-Ferrand, Clermont-Ferrand, Fr.
SOURCE: Drugs Aging (1999), 14(5), 337-345
CODEN: DRAGE6; ISSN: 1170-229X
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 49 refs. Prevention of levodopa-induced dyskinesias is a therapeutic challenge for physicians. At present, it seems only possible to delay dyskinesias and motor fluctuations. In younger patients (aged <50 yr), the strategy is to use a dopamine D2 agonist as monotherapy and then to add levodopa treatment when the parkinsonian symptoms progress. In older patients, (aged >50 yr to <70 yr), the therapeutic approach is to use early combination therapy of levodopa and a D2 agonist. The treatment of levodopa-induced dyskinesias must be considered in regard to the subtype and the severity of dyskinesias, and the patient. The general approach to the treatment of peak dose dyskinesias is to maintain dopamine brain stimulation at as stable a level as possible by keeping plasma and brain levodopa concns. in the therapeutic range (above the therapeutic threshold but below the dyskinesia threshold). An appropriate strategy is to reduce the individual dose of levodopa, to spread out the daily levodopa dose and/or to try treatment with the sustained-release form of the drug. Combination treatment with the std. and sustained-release levodopa formulations is also possible. Stopping selegiline (deprenyl) therapy may reduce dyskinesias; reducing the dose of, or stopping treatment with, a dopamine agonist may also be beneficial. Anti-dyskinetic drugs such as amantadine, buspirone, fluoxetine, propanolol and principally clozapine may be used. In severe dyskinesias, apomorphine infusion may be tried. In refractory dyskinesia, surgical procedures such as pallidotomy and chronic deep brain stimulation (globus pallidus/subthalamic nucleus) may be proposed. Theor., treatment of diphasic dyskinesias requires the maintenance of plasma levodopa concns. above the dyskinesia threshold. However, this approach leads to const. and severe dyskinesia after only a few weeks of treatment. Thus, the strategy used to treat diphasic dyskinesia is close to the treatment of peak-dose dyskinesias. Apomorphine (or the liq. form of levodopa) may be helpful to prevent diphasic dyskinesias. In selected patients, a midday rest in the "off" phase may decrease the duration of dyskinesia. Treatment of early morning dystonia is based on the addn. to the regimen of the sustained release formulation of levodopa before bedtime. Liq. levodopa and apomorphine injection may be used just before the appearance of the dystonic posture. Botulinum toxin may be helpful in severe dystonia.
REFERENCE COUNT: 49
REFERENCE(S): (4) Block, G; Eur Neurol 1997, V37, P23 CAPLUS
(10) Dupont, E; Acta Neurol Scand 1996, V93, P14 CAPLUS
(13) Durif, F; Neurology 1997, V48, P658 CAPLUS
(16) Gimenez-Roldan, S; Clin Neuropharmacol 1997, V20, P67 CAPLUS
(34) Papa, S; Ann Neurol 1996, V39, P574 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s parkinson's disease and l1

QUERY PROCESSING INTERRUPTED
The system was temporarily unable to process your query.  If this
message appears repeatedly, please notify the Help Desk.  Enter "HELP
STN" for information on contacting the nearest STN Help Desk by
telephone or via SEND in the STNMAIL file.

=> s parkinson's disease and l1

QUERY PROCESSING INTERRUPTED
The system was temporarily unable to process your query.  If this
message appears repeatedly, please notify the Help Desk.  Enter "HELP
STN" for information on contacting the nearest STN Help Desk by
telephone or via SEND in the STNMAIL file.

=> s parkinson? disease and l1

         10399 PARKINSON?
        381845 DISEASE
        119932 DISEASES
        443991 DISEASE
                 (DISEASE OR DISEASES)
          1729 PARKINSON? DISEASE
                 (PARKINSON?(W)DISEASE)
L2           0 PARKINSON? DISEASE AND L1

=> s parkison? disease

            25 PARKISON?
        381845 DISEASE
        119932 DISEASES
        443991 DISEASE
                 (DISEASE OR DISEASES)
L3           1 PARKISON? DISEASE
                 (PARKISON?(W)DISEASE)

=> s parkinson? disease

         10399 PARKINSON?
        381845 DISEASE
        119932 DISEASES
        443991 DISEASE
                 (DISEASE OR DISEASES)
L4        1729 PARKINSON? DISEASE
                 (PARKINSON?(W)DISEASE)

=> s ti 1-10

        232941 TI
           728 TIS
        233492 TI
                 (TI OR TIS)
       5462162 1
       2364814 10
L5           49 TI 1-10
                 (TI(W)1(W)10)

=> s parkinson? disease

         10399 PARKINSON?
```

```
        381845 DISEASE
        119932 DISEASES
        443991 DISEASE
                  (DISEASE OR DISEASES)
L6        1729 PARKINSON? DISEASE
                  (PARKINSON?(W)DISEASE)

=> d ti 1-10


L6   ANSWER 1 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Effects of chronic levodopa and pergolide treatment on cortical
     excitability in patients with Parkinson's disease: a transcranial magnetic
     stimulation study

L6   ANSWER 2 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Molecular mechanisms of late life dementias

L6   ANSWER 3 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Molecular etiology of Parkinson disease: recent
     progress

L6   ANSWER 4 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Stereospecific prevention by 17.beta.-estradiol of MPTP-induced dopamine
     depletion in mice

L6   ANSWER 5 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Variable absorption of carbidopa affects both peripheral and central
     levodopa metabolism

L6   ANSWER 6 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Dopamine transporter function assessed by antisense knockdown in the rat:
     protection from dopamine neurotoxicity

L6   ANSWER 7 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Ariadne-1: A vital Drosophila gene is required in development and defines
     a new conserved family of RING-finger proteins

L6   ANSWER 8 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Ferritin in nuclear magnetic resonance

L6   ANSWER 9 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Process for the preparation of alkyl mercapto methyl ergoline derivatives

L6   ANSWER 10 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
TI   Association of l-DOPA with recovery following Ayurveda medication in
     Parkinson's disease


=> d ibib 3


L6   ANSWER 3 OF 1729  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         2000:588200  CAPLUS
TITLE:                    Molecular etiology of Parkinson
                          disease: recent progress
AUTHOR(S):                Shastry, Barkur S.
CORPORATE SOURCE:         Eye Research Institute, Okland University, Rochester,
                          MI, 48309-4480, USA
SOURCE:                   Neuroscientist (2000), 6(4), 231-240
                          CODEN: NROSFJ; ISSN: 1073-8584
PUBLISHER:                Sage Publications, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

=> d his

(FILE 'HOME' ENTERED AT 19:43:57 ON 06 SEP 2000)

FILE 'CAPLUS' ENTERED AT 19:44:17 ON 06 SEP 2000
L1 1 S 131:85/DN
L2 0 S PARKINSON? DISEASE AND L1
L3 1 S PARKISON? DISEASE
L4 1729 S PARKINSON? DISEASE
L5 49 S TI 1-10
L6 1729 S PARKINSON? DISEASE

=> s 124:200109/dn

L7 1 124:200109/DN

=> d ibib abs

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:141217 CAPLUS
DOCUMENT NUMBER: **124:200109**
TITLE: HIV-1 infection of cultured human adult oligodendrocytes
AUTHOR(S): Albright, Andrew V.; Strizki, Julie; Harouse, Janet M.; Lavi, Ehud; O'Connor, Michael; Gonzalez-Scarano, Francisco
CORPORATE SOURCE: Deps. of Microbiology, Pathology and Lab. Medicine and Neurosurgery, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-6146, USA
SOURCE: Virology (1996), 217(1), 211-19
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mech. through which HIV-1 causes HIV dementia (HIVD) is not well understood. Myelin pallor is a common pathol. finding in HIVD and could be explained by a direct infection of oligodendrocytes or interaction with HIV-1 gp 120. To det. if oligodendrocytes could be infected by HIV-1, we purified oligodendrocytes from adult human brain tissue obtained from temporal lobe resections. These cells were exposed to HIV-1 and infectivity was assayed by detection of p24gag antigen, PCR amplification, and cocultivation with CD4+ cells. These results indicate that HIV-1IIIB and BaL and one of four primary isolates tested can infect oligodendrocytes, resulting in the prodn. of infectious virus. Furthermore, in an expt. that mimics a potential in vivo scenario, infected microglia were able to transmit virus to oligodendrocytes in a trans-well culture system. These expts. indicate that oligodendrocyte infection should be considered in studying the pathophysiol. of HIVD.

=> s 130:89983/dn

L8 1 130:89983/DN

=> d ibib abs

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:46416 CAPLUS
DOCUMENT NUMBER: **130:89983**
TITLE: New indications for thalidomide

AUTHOR(S): De Jong-van den Berg, L. T. W.; Rutgers, J.; Cornel, M. C.; Takx-Koehlen, B. C. M. J.
CORPORATE SOURCE: Groningen Inst. Drug Studies, Rijksuniv. Groningen, Groningen, 9713 AW, Neth.
SOURCE: Ziekenhuisfarmacie (1998), 14(4), 190-193
CODEN: ZIFAEM; ISSN: 0169-2720
PUBLISHER: Nederlandse Vereniging van Ziekenhuisapothekers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Dutch
AB A brief review with 38 refs. is given on new indications for thalidomide. Besides the beneficial effects of thalidomide in erythema nodosum leprosy the drug is efficacious in other major disorders such as aphthae and ulcers in aids, tuberculosis, autoimmune diseases, and tumors.

=> s 119:179060/dn

L9 1 119:179060/DN

=> d ibib abs

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:579060 CAPLUS
DOCUMENT NUMBER: **119:179060**
TITLE: In vitro tumor necrosis factor production by mononuclear cells from lepromatous leprosy patients and from patients with erythema nodosum leprosum
AUTHOR(S): Santos, Dilvani O.; Suffys, Philip N.; Bonifacio, Karla; Marques, Maria A.; Sarno, Euzenir N.
CORPORATE SOURCE: Dep. Cell. Mol. Biol., Fed. Fluminense Univ., Valonguinho, 20400, Brazil
SOURCE: Clin. Immunol. Immunopathol. (1993), 67(3, Pt. 1), 199-203
CODEN: CLIIAT; ISSN: 0090-1229
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prodn. of tumor necrosis factor (TNF) by Mycobacterium leprae-stimulated phagocyte cells, isolated from lepromatous leprosy patients (LL) and normal individuals, was evaluated, using the highly TNF-sensitive mouse fibrosarcoma cell line WEHI164cl13. Mononuclear cells, isolated from all individuals studied, showed a low level of spontaneous TNF prodn., except for patients undergoing erythema nodosum leprosum (ENL), in which the authors found significantly higher levels of TNF. Addn. of M. leprae to the phagocyte cell culture enhanced TNF prodn. in all groups studied, except in the group with untreated leprosy patients. Strongest M. leprae-induced TNF release was found in mononuclear cell cultures derived from ENL patients. Patients in the postreactional state showed significantly higher TNF levels than healthy controls. These findings support the idea that TNF plays a key role in the complex symptomatol. of ENL.

=> s erythema nodosum leprosy

2757 ERYTHEMA
36 ERYTHEMAS
2781 ERYTHEMA
(ERYTHEMA OR ERYTHEMAS)
534 NODOSUM
1297 LEPROSY
L10 2 ERYTHEMA NODOSUM LEPROSY
(ERYTHEMA(W)NODOSUM(W)LEPROSY)